English Edition 190,000

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

18706

Vol. IV **1919** **No. 1**

CONTENTS

The New Metabolist.................... 1
Present Status of Organotherapy........ 1
Animal Protein in the Diet............ 3
Post-Graduate Medical Instruction in America.......................... 5
Thyroid Toxemia and Exophthalmic Goiter............................ 5
The Predetermination of Sex........... 6
Lowered Resistance and Influenza....... 6
Diet and Milk Secretion............... 7
Function of the Adrenal Cortex......... 8
Glycosuria in Elderly Persons........... 9
Prevention and Treatment of Diabetic Coma............................ 9
Calomel in Spanish Influenza........... 13
Correlation of the Internal Secretions in Regard to Their Genital Functions.... 14
A Brief Study of Goiter................ 15
Observation on Three Cases of Scurvy... 16
Observations on the Cause of Rickets.... 16
Pituitary Headaches and Their Cure..... 17
Saline Solution with Organ Extracts in Shock.............................. 18
The Manic-Depressive Constitution..... 18
The Co-operation Between the Spleen, Thyroid and Bone Marrow........... 19
Vitamines as Factors in the Diet........ 20
The Effect of the Maternal Ingestion of Desiccated Placenta upon the Rate of Growth of Breast Fed Infants........ 20
Relative Content of Anti-Scorbutic Principle in Limes and Lemons........... 21
Book Reviews......................... 22
Items of Personal Interest.............. 23

The Pluriglandular Tonic For Asthenic Conditions

HORMOTONE

INDICATIONS: Neurasthenia; "run down" conditions; suboxidation; neuroses; menstrual and climacteric disorders; cardiac asthenia; low blood pressure.

In neurasthenia associated with high blood pressure and all hypertensive conditions use **Homotone Without Post-Pituitary.**

Dose: One or two tablets 3 times daily before meals.

LITERATURE ON REQUEST.

G. W. CARNRICK CO., 13-15 Laight St., New York City

HIGH BLOOD PRESSURE

As far as medication in the treatment of high blood pressure is concerned, there is little doubt but that organotherapy offers a field of much promise.

Opportunity is here given to the practitioner to correct duodenal, hepatic and pancreatic insufficiency which causes an undue intestinal putrefaction. The toxins arising from this putrefaction stimulate the suprarenal glands to increased function with a consequent rise in the blood pressure.

Where the high blood pressure is an accompaniment of middle age there are often in both sexes, thyroid and gonad insufficiencies to be corrected.

SECRETOGEN AND TRYPSOGEN

The use of Secretogen and Trypsogen to correct abnormal conditions of the intestinal tract is followed by remarkable improvement. These patients should get two or three Secretogen Tablets before meals and two or three Trypsogen Tablets after eating. Where the high blood pressure is associated with albuminuria, *Trypsogen without gold and arsenic* should be used. To combat the thyroid and gonad insufficiency

HORMOTONE WITHOUT POST-PITUITARY

will be found of great service. The dose of this preparation in the treatment of high blood pressure is 1 or 2 tablets three times daily before meals.

In the adjoining column will be found convincing clinical reports as to the efficacy of these three organotherapeutic products in the treatment of arterial hypertension.

Organotherapy in this condition is theoretically indicated and of practical benefit.

CLINICAL REPORTS

"Aug. 1, 1915.

"*Gentlemen:*

"Allow me to thank you for sending samples of Secretogen and Trypsogen and report that my blood pressure is nearly normal and the albumin has entirely disappeared. You can imagine my surprise when after two years of constant dieting and using every medicine known in and out of the Pharmacopeia I found my urine free of albumin. The only additional medication was about one quart of Vichy daily. My doctor friends can hardly believe this."

"Nov. 25, 1918.

"*Gentlemen:*

I have been using Secretogen and Trypsogen in cases of high blood pressure according to your suggestion in a late number of *The Metabolist*, and I am highly elated over the results. I placed five cases on this treatment and three of them were lowered to normal or nearly so in two weeks and have remained so. The other two were cases of much longer standing as organic changes had already taken place. These two cases have been benefited to the extent of having their inordinate appetite reduced to normal proportions, and one of them has had his pressure reduced quite a bit."

The following letter from the English clinician Dr. T. Bodley Scott, is of decided interest:

"You were so good as to put on the market some time ago, partly I believe in consequence of an article of mine in *The Practitioner*, a new Hormotone Tablet which contained no Post-Pituitary. This I have found very valuable, as one can give it freely in elderly people whose blood pressure is above normal. I have found that your Hormotone Without Post-Pituitary not only does not raise pressure, but that it has a decided effect in lowering it. In nearly all my cases in which a gradual reduction of pressure is wanted, I think it is one of the most valuable remedies we have. The nitrites, of course, produce the more immediate effect, but one not nearly so lasting. Hormotone Without Post-Pituitary causes no gastric disturbance like the iodides, and no headache like the nitrites."

In *The Practitioner* for November, 1917, Dr. Scott again refers to the value of Hormotone Without Post-Pituitary. He cites an astonishing case in which "The patient apparently being *in extremis*," Hormotone Without Post-Pituitary had a surprisingly good effect."

"December, 1918.

"*Gentlemen:*

"Please send me two bottles of Hormotone Without Post-Pituitary. I find them most valuable for elderly people suffering from high blood pressure. In some cases one or two a day are quite sufficient to get rid of the headache and frequency of micturition which so often are caused by high blood pressure."

SECRETOGEN

The natural, wholesome way to treat

INDIGESTION AND CONSTIPATION

is to furnish the stimulating and nutritious material to the glands which elaborate prosecretin and the ferments needed in normal digestion.

Secretogen does this — and more.

It is of great service in those cases of constipation that are due to biliary insufficiency and deficient tone of the nervous and muscular mechanism of the intestine.

A high authority on diseases of the stomach writes: "Elixir Secretogen is apparently the most powerful excitant of gastro-intestinal secretions so far tried by me. I find that Elixir Secretogen is much more active than the standard pepsin and HCl mixtures, and that its action upon the production of gastric juices is not limited to the influence which immediately follows its administration. I have examined chemically the stomach contents of one of the patients referred to in which none of the Secretogen Elixir had been taken for a month and the proportions of both free and combined HCl were found to be still a little above normal, though before the remedy was taken there had been no HCl at all, and the proportions of both the combined HCl and of the total acidity had been decidedly below normal."

"September 15, 1918.

"I should like to say that I have found Secretogen most effective in many cases of dyspepsia during the past four years; cases which did not readily respond to the usual remedies."

OUR CREED

We believe in Organotherapy; we believe that it ushers in the dawn of a better day in the treatment of disease.

We believe that an intelligent understanding of physiology, with its conception of the normal workings of the animal organism, offers a more hopeful outlook than the "horrible examples" of pathology, and that the latter is valuable only in that it teaches us to appreciate the former.

We believe that animal products, properly prepared, give the physician one of the most effective weapons he can wield in his warfare against the ever-increasing disorders of metabolism.

We believe in ourselves; in our ability to prepare these products; in our good faith in presenting them; and in our honesty in marketing them.

G. W. CARNRICK CO.

"Mr. A. —— several years ago, had a serious typhoid fever, and every year since, beginning in the early summer, he has developed a gastrointestinal condition, first starting as a diarrhoea, running on through the summer until a general enterocolitis develops, with frequent bloody and mucous stools which has entirely incapacitated him for some months in each year. He has had the best medical advice of — —, and — — cities. Last June he consulted me at the beginning of his trouble. I prescribed Secretogen Elixir, to which he promptly responded, and he has passed through the summer on an unrestricted diet with no return of his annual illness.

"Mrs. T.—— who has had a chronic diarrhoea for ten years and who had to be restricted to the simplest non-irritating diet, found prompt relief about two years ago from Secretogen.

"I have treated two other cases with equally satisfactory results and I am grateful to you for having given to the profession so valuable a remedy."

"I have experimented with both Secretogens and find they work like magic. The results are immediate and very pronounced. The taste of the Elixir is most delicious and it is a temptation not to take more than the prescribed dose. I expect to use a great deal of the remedy."

SECRETOGEN

is prepared in two forms:

Elixir Secretogen: A physiological stimulus to the stomach, pancreas, liver and intestinal glands. Dose: 1 to 4 teaspoonfuls before meals; children in proportion.

Secretogen Tablets: A physiological stimulus to the pancreas, liver and intestinal glands in functional digestive disorders of the intestinal tract.

Dose: 1 to 4 tablets before meals; children in proportion.

ORGANOTHERAPY IN GYNECOLOGY

Some one has sagely said: "Take care of the women and your practice will take care of itself."

Probably 30 per cent. of the patients treated in general practice are women suffering with some derangement of menstrual or generative functions.

Up to the age of puberty there is little or no difference in the metabolism of a boy or a girl. At that time, however, striking changes in the contour and other physical characteristics of the body take place. The distribution of hair on the body is sharply differentiated in both sexes, and the fact that a man shaves himself while his wife doesn't have to is dependent upon the difference in their internal secretions. The same may be said of the development of the breasts, the texture of the skin, the weight and length of the bones, the difference in the pitch of the voices, the distribution of fat, and last — but not of least importance — the psychic expression of the individual. All of these depend upon the glands of internal secretion. This applies not only to the sexual glands but to the other glands physiologically bound up with the normal functioning of the ovary or the testis. This is especially true of the thyroid and the pituitary. With diminished efficiency of the thyroid there can be no normal functioning of the sexual apparatus and the same may be said of the hypophysis. Further, realizing the importance of these glands of internal secretion in the normal sexual life of the individual, it follows logically that extracts of them may be used to advantage in restoring normal conditions of the procreative mechanism.

Owing to the reciprocal relationship that exists between the glands of internal secretion, a functional disorder of them is, in its last analysis, always a pluriglandular disturbance — never a monoglandular malady. While it is true that the predominant symptoms may be characteristic of a disorder of the gland that is chiefly affected, it is also true that the involvement of the other glands is just as important. They may have been acted upon by the first gland but in turn they have reacted on it. The glands which are intimately associated with the development, the nutrition and the tone of the female genital system are the ovary—the thyroid and the hypophysis. Blair Bell believes that the suprarenals also influence the development and preserve the activity and integrity of the genitalia. In any event, a combination of gland extracts containing thyroid, pituitary and ovary is indicated in functional disorders of the female genital apparatus and better results do, in fact, follow the use of pluriglandular preparations.

Hormotone: A particularly effective combination is offered under the name Hormotone, which contains the hormones of the thyroid, pituitary, ovary and testis. Each tablet contains 1/10 grain of desiccated thyroid and 1/20 grain of entire pituitary.

Hormotone causes an increase in mental, nervous and muscular activity. It is indicated in the disabilities incident to old age; lowered virility and the sexual neuroses of the unmarried; it is also of great value in amenorrhea, dysmenorrhea and hysteria following functional exhaustion of the nerve centers. In all diseases attended with suboxidation it will be found of distinct service.

The functional disorders that are amenable to treatment with Hormotone include amenorrhea, dysmenorrhea, natural or surgical menopause, menorrhagia, metrorrhagia, infantilism, sterility, anemia, chlorosis, hysteria, metabolic disorders associated with obesity and frigidity.

W. P. Graves, *Gynecology*, page 56, says: "Amenorrhea, or oligomenorrhea, that is seen in fully developed women who have previously menstruated normally, is accounted for as a result of functional ovarian insufficiency, a theory that finds strong confirmation in the almost immediate beneficial effect which ovarian extract usually has on these cases." However, the association of the thyroid with the sexual apparatus is well known and, bearing in mind that thyroid disturbances are ten times as common in women as in men, the importance of normal function of this gland in the female economy is readily realized. Various French observers, such as Leopold Levi, de Rothschild, and Collard-Huard have clearly demonstrated the interdependence of the thyroid, the ovary and menstrual phenomena.

Hormotone has given very good results in the treatment of amenorrhea.

In dysmenorrhea where there is no mechanical hindrance to the distention of the ovaries and uterus during the menstrual congestion and where there may be defective development, abnormal ovulation, or other causes for the condition, the source should be sought in the glands with an internal secretion, especially the thyroid. It has long been known that there is a direct relationship between the function of the thyroid gland and dysmenorrhea.

Dalché has recommended thyroid and ovarian extracts given alternately for this condition. Two other French clinicians, Siredey and Lemaire recommend pluriglandular therapy consisting of extracts of the thyroid, ovary and pituitary glands. Pluriglandular therapy is more effective in this condition than the use of single extracts even if hypothyroidism is the most pronounced symptom accompanying the disorder.

A fertile field for the use of Hormotone is any disturbance associated with the menopause. Blair Bell says: "The way seems clear to the solution of the problem which has so long troubled us — the question of a substitution product in ovarian insufficiency. It seems certain that ovarian extract alone is of little value — in spite of a few favorable reports — because after ovarian atrophy or removal, the other endocrinous glands are affected . . . so that ovarian extract alone is not sufficient to combat all the metabolic disturbances. If, however, we use our knowledge of the correlated changes in other glands, before long we shall find a combined extract that will give us some measure of success. I believe that the treatment of menopausal disturbances lies in the suitable use of the extracts of endocrinous glands other than the ovary, alone or in conjunction with ovarian extract." (*Proc. Royal Soc. Med.*, Sec. Obs., 1913, pp. 55, 67). Bandler says that in the climacterium there is a progressive failure on the part of the ovaries to produce their normal secretion, that alterations occur in other glands in the body, the thyroid being the one most particularly involved. He further states that if the ovary and thyroid diminish as to the secretion which they produce in equal ratio, the patient goes through her menopause calmly and without upset. If the ovarian function diminishes with too great rapidity and that of the thyroid too slowly the patient is in the state of hyperthyroidism. If thyroid function diminishes too quickly the patient may be in a state of hypothyroidism. In the latter case there is a tendency to a high blood pressure in which condition Hormotone Without Post-Pituitary should be used.

It is known that the beginning of the menopause is accompanied by important changes in the structure of the thyroid body. Starting from the basis that certain disturbances of the menopause may be due to thyroid insufficiency, Perlisse has used thyroid extract in small doses in the treatment of these cases. Pituitary extract has also given good results in the treatment of menorrhagia and in hemorrhages of the menopause the associated gland extracts which go to make up Hormotone will be found particularly effective.

Both thyroid and pituitary extract have been used in the treatment of uterine hemorrhages. Sehrt found in 55 cases of uterine hemorrhage, without any discoverable local cause, that 38 of the patients had all the signs of pronounced thyroid hypofunction. In every case marked benefit was derived from thyroid treatment. Pituitary extract exercises its good effects in such cases probably from the correction of the atony of the uterine muscle rather than from the correction of any inherent pituitary insufficiency.

In cases of sexual infantilism, there may be thyroid or pituitary insufficiency or both. Brissaud and his followers have claimed that all cases of infantilism can be ascribed to a deficiency of the normal activity of the thyroid gland. Most observers deny this. In any event with thyroid insufficiency sexual development is much delayed and secondary sex characters are sometimes absent. The result of pituitary insufficiency in these cases leads to changes in the distribution of the hair which becomes scanty on the scalp and in the pubic and axillary regions and tends to grow low down on the forehead and in front of the ears. In these cases you may have mental dullness, sleepiness, sometimes irritability, and often epilepsy.

Weil speaks of the results of thyroid therapy in the treatment of sterility and holds for special consideration the apparent correlation between the thyroid and the ovaries; he advocates the use of thyroid preparations in sterility due to ovarian insufficiency. He exhibited the remedy in two barren women, who, aside from a slight enlargement of the thyroid, showed nothing to suggest a reason for failure to conceive. After several months conception took place in both women. The same has occurred after the exhibition of Hormotone.

In anemia with general asthenia and suboxidation, ovarian preparations have proved themselves of value and, in this connection, it is well to state that stimulation of the suprarenal system is a prime factor in overcoming the condition. Several clinicians have used ovarian preparations in chlorotic girls where a hypoovarism was demonstrable. There are more factors to be overcome in this condition however, and the other constituents in Hormotone by the promotion of suprarenal efficiency stimulate oxidation and overcome the blood dyscrasia.

Several instances are on record where ovarian extract has been given with success in the treatment of hysterical crises, and one case has even been recorded where transplantation of ovarian tissue from a patient on whom hysterectomy had been performed, to a patient suffering from mental disorder due to ovarian disease, was followed with the happiest results. Hormotone has given satisfaction in the treatment of hysterical and melancholic conditions.

At the time of the menopause, obesity is very often one of the most pronounced symptoms, and is often accompanied by a hypothyroidism with a high blood pressure, although an asthenic condition may be met with. It is also recognized that a diminution of the internal secretion of the ovaries has much to do with the onset and development of obesity. Hence the use of a preparation containing thyroid, ovarian and testicular substance, with its well-known stimulating effect upon metabolism and oxidation, is rational. Where the obesity is accompanied by a hypotensive condition, Hormotone should be used, and where the condition is accompanied by a high blood pressure, Hormotone Without Post-Pituitary should be prescribed.

The condition of frigidity is the cause of much unhappiness in the married state, and it is reasonable to assume that treatment with Hormotone would be indicated. This has proved to be the case. Not only do the thyroid and ovarian extracts in the preparation stimulate the tone of the genital organs, the pituitary extract is also indicated because this gland is probably the most important factor in the nutrition and maintenance of tone in the sexual apparatus.

TIME TELLS THE TALE

The past twenty years have seen the advent and the passing of many preparations offered in the therapy of

DIABETES MELLITUS

Only one preparation has passed through the clinical ordeal, not only unscathed, but with its prestige increased. The value of

TRYPSOGEN

has been very thoroughly demonstrated by the results which have accompanied its use in all parts of the world. The number of physicians who are using Trypsogen systematically in the treatment of diabetes mellitus is steadily increasing.

Trypsogen is a medicinal adjuvant of value to the dietetic and hygienic measures generally advocated in the treatment of this disorder.

In cases of diabetes mellitus complicated with albuminuria

TRYPSOGEN WITHOUT GOLD AND ARSENIC

should be specified.

Dosage: One or two tablets after each meal. Dose should be gradually increased until the patient is taking five, six or seven tablets after eating. On account of the large dosage and persistent treatment bottles of 500 should be prescribed if possible.

Trypsogen is stocked by most wholesale and retail druggists in all English speaking countries.

Some recent clinical reports from physicians are appended in the adjoining column.

G. W. CARNRICK COMPANY

New York **London**

CLINICAL REPORTS

"I think it only fair to write you regarding the Trypsogen purchased some five years ago. I discovered that I had quite a severe attack of diabetes and of course tried many of the accepted remedies, with but little benefit however. I took altogether about 600 tablets of Trypsogen with the result that I have had no symptoms of the trouble since.

"I feel satisfied that some of the failures with Trypsogen medication have been due to insufficient dosage. I took them in doses large enough to cause a frontal headache; my recollection being that I took about 25 to 30 tablets daily. Excepting proper diet, Trypsogen constituted the entire treatment."

"In reply to your favor I would advise you that since I purchased 1500 tablets of Trypsogen, I have fully recovered from diabetes and am now in perfect health, — having fully resumed my busy practice, am active and vigorous."

"The Trypsogen you sent me I am giving to a patient with diabetes. The carbohydrate limit which before taking Trypsogen was 21 grams has now been gradually increased to over 50 grams per day without showing a trace of sugar in the urine."

"I used Trypsogen on a case of diabetes mellitus which had so progressed that when I first saw her I was willing to bet 50 to 1 that part of the toes on one foot had to be amputated on account of gangrene.

"Under Trypsogen she got well and no operation was performed. I now prescribe Trypsogen frequently."

"I have no doubt of the value of Trypsogen. I have found that it certainly 'lessens polyuria' and 'materially improves digestion' as stated in your letter."

"I make extensive use of Trypsogen. I have just treated a bad case of diabetes in which the trace of sugar has disappeared and the patient is steadily gaining in weight and strength. In a practice of over 50 years I have never found any remedy for diabetes mellitus that can be compared to Trypsogen."

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

BOSTON MEDICAL
AUG 27 1920
LIBRARY

Vol. IV **1919** **No. 1**

THE NEW METABOLIST

Beginning with this issue, THE METABOLIST has been increased in size. Its editorial staff has been enlarged and we have secured the services of an accomplished and experienced translator of foreign medical literature whose entire time is devoted to this work.

THE METABOLIST has much the largest circulation of any medical journal now issued, being published in three languages and reaching 230,000 physicians.

Many of the best papers on organotherapy in English appear in scientific medical publications of high price and small circulation; others in French, Italian and other foreign journals. Very important discoveries in organotherapy for this reason are not as a rule brought to the attention of the mass of practitioners until years have elapsed.

To publish and distribute such a journal as this to 230,000 physicians every three months is an ambitious undertaking for a pharmaceutical house, but in this day *service is the road to success.* And we believe we shall be able to publish a journal worth reading and keeping.

In order to be well informed in the field in which we specialize, we have for the past 19 years been collecting, translating, classifying and collating the published researches and articles relating to hormones, internal secretions, nutrition, metabolism, and the therapy of associated diseases. Practically every special scientific and general medical journal in English, French, Italian, Spanish and German is regularly reviewed and contemporary contributions and abstracts from these sources will be presented to readers of THE METABOLIST.

THE PRESENT STATUS OF ORGANOTHERAPY

That precocious youngster, organotherapy, is just about to emerge from the kindergarten stage. Born centuries upon centuries ago, myxedemic, deaf, dumb and blind, the plaything and tool of near-wise men and witches, the poor infant was the stock-in-trade of many a charlatan.

Rescued in the 19th century by such men as Claude Bernard, Brown-Sequard, and G. R. Murray, the infant was slow in recovering from this deplorable condition and although her virtues have been for the most part appreciated by empirical methods, there is little reason to doubt that in the not distant future there will be a better basis for organotherapy because it will be scientific.

The field of usefulness of glandular extracts appears to be virtually limitless. To be sure, their present use is based for the most part on clinical experience, but they undoubtedly are remedies of the greatest potency.

Hitherto the medicinal treatment of disease has been carried out by the use of drugs; that is, of substances which are foreign to the animal organism. The action of these drugs is often difficult of explanation, still more difficult of regulation. This may be said of almost every item of vegetable origin in the pharmacopœia, but is, of course, less true of inorganic remedies. Many of these salts are not foreign to the organism and the dose of them can be more accurately measured. For instance, the salts of sodium, potassium, calcium, magnesium and iron already exist in the body and may be classed as nutritive substances rather than drugs.

In contradistinction to drugs, when we are using animal extracts we are using principles that are indigenous to the soil in which they are being employed. That, in itself, gives the products used in organotherapy a great advantage over the other remedies that have been used for ages in the treatment of disease.

As to the methods of administration of these potent remedies, there is great diversity of opinion. The controversy reminds one of the old threadbare discussion as to the therapeutic availability of pancreatic enzymes given by mouth and unprotected from the stomach fluids. Despite the conclusions of test-tube authorities, no less a worker than Brieger, a very competent physiological chemist, in recommending the use of pancreatic enzymes in the treatment of tuberculosis, says that no attempt should be made to protect the product from the effects of contact with the stomach secretions. He recommends that the pancreatic extract should simply be put upon the tongue from the end of a knife blade. Any physician who has used pancreatin systematically in his practice can confirm the value of Brieger's recommendation.

The reason why oral administration in experiments on animals in physiological laboratories is not in favor is that one can never be sure that the preparation is properly swallowed or that the dosage by mouth is as it should be. And again it has to be remembered that in laboratory experimentation the animals are usually in normal health and that being the case, it is obviously absurd to expect results from the administration of organotherapeutic products as compared with the efficacy of these remedies in diseased conditions.

In this connection the late William A. Hammond said: "All the organs of the body possess the power, when in a state of health, of secreting from the blood the peculiar substance that they require for their nutrition, and they take this substance, and no other, never making a mistake in the matter. The brain separates brain substance; the heart, heart substance, and so on. If, through disease, or from derangement of function, they lose this power, or if the peculiar pabulum they require be not in the blood in sufficient quantity, their functions cease to be normal. . . . If we supply to the blood the peculiar principle which a diseased or disordered organ requires, we do that which nature, unassisted, cannot, or does not do."

In *La Pratique de L'Opotherapie* Hallion points out that "the opotherapeutic product which corresponds to the affected organ represents in some way the stimulating and elective food for that organ, and if we supply the organ with a food which is more complete than it necessarily needs, the affected organ can exercise its elective action and take up only those substances of which it is in need.

As to the particular use of gland extracts, they are of value to the physician in various ways. They may be used for diagnostic purposes. If a physician is led to believe that his patient is suffering from hyperpituitarism or hyperthyroidism he may give pituitary or thyroid extract, and in the event of his assumption being correct the patient's symptoms will become aggravated. The same is true if he suspects hypopituitarism or hypothyroidism. If the patient improves he may be sure that he is on the right track. Still another instance is differentiating in the variety of constipation from which a patient may be suffering. If the bowel muscle is paretic pituitary extract would restore its irritability. In other forms of constipation it would be of no value.

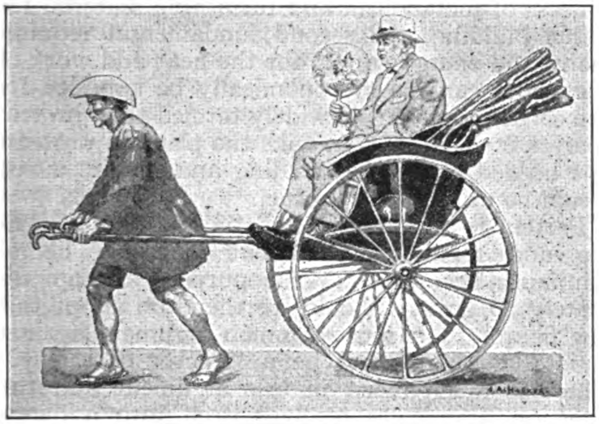
Further, a physician may use the extract of a gland to make up for a deficiency of secretion in that particular gland as in the case of thyroid in myxedema; this is purely substitutive organotherapy. Again, an extract might be used for its homo-stimulative properties, as in minor hypothyroidism where the gland is only functionally inactive. He might also use an extract for its heterostimulative properties, such as small doses of thyroid for the effect on the ovaries or the adrenals. In this instance an extract of the particular gland that is being used is acting as a true hormone.

Still again a gland extract may be used for the inhibitory effect it has on other glands, such as mammary extract on the ovaries and pancreatic extract on the adrenals. The term chalone is used for those internal secretions which act in this inhibitory manner.

Of the organotherapeutic agents indicated in general practice, Sajous says that his preference has always been for the desiccated gland in powdered form. This is of the highest importance because, unless one treats a condition in a purely symptomatic way, such as giving adrenalin or pituitrin in shock, it is better to give a total extract of the gland. We do not know, for instance, how many therapeutic principles are contained in adrenal substance, for adrenalin is only one of its many entities and adrenalin no more represents adrenal substance than codein does opium.

As to the measure of success that will attend organotherapy, it will be found that the most striking results will be obtained in those subtle disorders that are not easily apparent on the surface. The more striking the objective evidence the less likely is benefit to be obtained. The great field of usefulness in organotherapy will not lie in such disorders as myxedema, mongolism, scleroderma or such easily apparent diseases, but in conditions like minor hypothyroidism, hypopituitarism and hypoadrenia. In these conditions lie a rich mine for the general practitioner as well as the specialist, but the treasures to be gained therefrom will only be had by the most painstaking investigation.

A physician who would be abreast of the times will have to grasp as thoroughly as possible the principles of organotherapy. There is no question but that it has come to stay and the results attained will be satisfactory both for the practitioner of medicine and for the many chronic cases which have hitherto sought relief in vain.



ANIMAL PROTEIN IN THE DIET

It has been said that the grain needed to produce beef enough to feed one man would maintain ten men.

The economic importance of such a statement is seen at a glance, but the relation of excessive meat eating to the causation of disease is not quite as apparent though just as real.

There is perhaps no more striking example of the adherence to instinctive rather than to intellectual dictates which characterizes human action than the tenacity with which a great percentage of the prosperous nations cling to a high animal protein diet. Notwithstanding the fact that practically every scientific research in recent years indicates that we eat as a rule from two to three times as much protein as is needed, it is with the utmost difficulty that even medical men are persuaded to change to the lower standard.

The contention of those who hold that the race cannot safely or wisely disregard its instinctive tendencies and who point to the fact that mankind, civilized and aboriginal, has adopted the higher protein requirement, is aptly met by Prof. Otto Folin (British Medical Association, Toronto, reported in *St. Tom's Medical Review*, Oct. 20, 1906) who objects to such argument "from habit" and says "it would equally justify such harmful things as tea, coffee, tobacco and alcohol." And if the instinct for meat eating was to be followed that against working would also be in logical order.

J. J. R. Macleod (*The Journal of Laboratory and Clinical Medicine*, August, 1917) says: "This discrepancy between the amount which experiment demonstrates to be adequate and that which habit and custom demand raises the question as to whether, after all, our instincts may not have erred and so made us unnecessarily extravagant in our protein intake."

The nutrition requirements determined by Carl Voit of Munich in his pioneer researches have been generally accepted. His requirement for individuals of average weight (70-75 kilos) and performing moderate muscular work is

Protein....... — 118 grams = 483.8 calories
Fat.......... — 56 grams = 520.8 calories
Carbohydrates — 500 grams = 2050.0 calories

and a total fuel value of 3054.6 large calories. It is against this 118 grams of protein that criticism must be directed.

Experiments, notably those of Chittenden (*Physiological Economy in Nutrition*) demonstrate that nitrogen equilibrium and a normal state of efficiency can be maintained upon a diet containing 30 to 50 grams of protein per day. McCay in his studies of the "Bengalis of India" finds that average weight of protein metabolized is about 37.5 grms. per day. The results of Prof. Hindhede of the Nutrition Laboratory of Copenhagen are even more convincing. In one case studied by him physical well-being was maintained for over a year, on a diet of potatoes, margarine and water.

It has been repeatedly demonstrated that not only are the carbohydrates alone sufficient for the energy needs of the body, but there is abundance of evidence to show that excessive meat eating is not compatible with prolonged muscular work. The case of the jinrikisha men employed by Prof Baeltz (*Protein and Nutrition*, Hindhede) is suggestive:—

"I had two jinrikisha-men; two powerful young fellows, one twenty-two, the other twenty-five years of age. They had followed the same calling for years. I provided their food, which was exactly measured, what they ate, and what they drank; and the chemical composition of the food was ascertained by recognized means. These men received definite instructions:— Every day for three weeks they had to drag me, a man weighing 80 kgs. (176.4 lbs.), a distance of 40 kms. (24.84 miles), running all the time. That appears to be a fairly arduous task— but not more so than that which these men would have willingly undertaken. But for my purpose it was quite enough; for we considered a walking expedition of 40 kms. as something quite respectable; but for a man to run 40 kms. every day throughout a sunny August is rather more than one would usually expect of us.

Now the men, during the experiment, kept to their usual diet, which contained fats amounting to less than half that proposed by Voit, while the contained protein fluctuated from between 60 to 80 per cent of his postulate. Carbohydrates, on the other hand, were provided in exceedingly large quantities, in the form of rice and potatoes, barley, chestnuts, lily-roots and other foodstuffs peculiar to the country. After fourteen days I weighed the two men. One had not made any change, while the other had added half a pound to his weight. After the fourteenth day I told the men I wished to give them meat. They were delighted, for meat is a luxury to them. I therefore substituted for a part of the carbohydrates a proportionate quantity of protein— not quite so much as Voit demanded, but a considerable amount. The men ate it with avidity; *but after three days they came and asked me to* *discontinue the meat, and to give it to them only upon the conclusion of their probation, because they felt so fatigued, and could not run so well as before.*"

Another instance is quoted from Professor Fisher in *Munsey's Magazine*:— "The flesh-eaters were largely men in training for athletic contests at Yale; the flesh abstainers were such Yale students as I could find who did not use meat, or used it very sparingly, and nurses and physicians of the Battle Creek Sanitarium. Forty-nine subjects were tested. The results of the comparison were certainly surprising, and showed almost conclusively that those who used low protein and little or no flesh, not only had greater physical endurance, but far greater than those who were on a so-called "training diet."

Very few of the flesh-eaters, for instance, could endure holding their arms horizontal for more than a quarter of an hour, whereas it was common among the flesh-abstainers to hold them for more than an hour, and without as much pain or discomfort as the meat-eaters experienced in half the time. In one case a flesh-abstainer held his arms out for three hours and twenty minutes, and then stopped merely because he had reached a round number of minutes — two hundred.

One of the most severe tests was in deep knee-bending, or "squatting." Few of the meat-eaters could "squat" more than three hundred to four hundred times, and it was almost impossible for them to walk down the gymnasium stairs, after the test, without falling, so weakened were their thigh muscles. On the other hand, one of the Yale students who had been a flesh abstainer for two years did the deep knee-bending eighteen-hundred times without exhaustion, after which he ran without difficulty on the gymnasium track and walked several miles. Another subject, a nurse at the Battle Creek Sanitarium, did the deep knee-bending twenty-four hundred times; after which he proceeded with his regular work without serious inconvenience. Another nurse has recently accomplished the surprising record of five thousand times. One remarkable difference between the two sets of men was the comparative absence of soreness in the muscles of the meat-abstainers after their tests."

It is well established that nitrogen balance may be established at different levels; as low as 30 grms., and as high as 2,500. The excess over basal metabolism requirements is deaminized in the body and used as an energy and heat producer — mere fuel of the most expensive kind taken in the human diet. The heat and energy of the body should be developed from the carbohydrates and fats.

It has been shown that the proteins are broken up and the nitrogen excreted as urea and the remainder of the molecule may be synthesized to carbohydrates and thus used in the same manner as similar material from the digestive products.

After the first great requirement of a food has been met — that of replacing tissue lost by the process of metabolism and furnishing material for tissue building, the second fundamental requirement, and energy supply for the heat and work of the body, can most economically be supplied by the carbohydrates now widely termed the "protein sparers." That is, they take the place of proteins not needed for tissue building and repair, which would be utilized only as fuel.

Protein is an absolute essential for tissue building and repair. Experiment places a liberal minimum necessary for the purpose at approximately 50 grms. Should we therefore adopt this low figure? The most common argument against it is that there must be a "Factor of safety." There is much merit in this argument and the question practically resolves itself into a determination as to what constitutes a reasonable "factor." Is from 2½ to 3 times the total amount required, necessary for safety? A review of current opinion leads us to believe that this is far too high. The conservative opinion of Prof. H. C. Sherman (*Food Chemistry in the Service of Human Nutrition, N. Y. Med. Jour*, Jan. 26, 1918) is worthy of careful consideration. He believes that the adoption of a standard protein allowance 50 per cent. above the average protein requirement would be an ample provision for all save growing children and nursing women. This would make a standard requirement of 75 grams. — a great saving over the 118 grams set by Voit and particularly important when we consider that it has been estimated that it multiplies the cost ten fold to feed carbohydrates to animals and supply an equivalent nutritive value as protein to the human consumer.

It is, moreover, important that we consider the relation of excessive protein intake to disease. An editorial in the *Medical Record* of April 1, 1918, epitomizes present thought on this subject. The consumption of too much protein unquestionably accelerates the progress of the degenerative diseases of heart, arteries and kidneys.

The mechanism by which such changes are accomplished is not entirely clear, but the causal relation seems certain. The potential danger in every protein molecule is now generally appreciated, due in great measure to the exhaustive investigations of Vaughan. It is known that every protein molecule contains a poisonous group which in all proteins is identical or closely similar in action. The toxicity of this poison may be appreciated in the light of Vaughan's statement that "from 1 gram of casein enough of this poison can be obtained to kill 800 guinea pigs when injected intravenously." (*Jour. A. M. A.*, Nov. 25, 1916.

L. F. Bishop (*Arteriosclerosis, Oxford University Press*, 1914), says: "The key to the riddle of arteriosclerosis, I believe, lies in just this sensitization of individuals to particular proteins or, to be more specific, to split products of particular protein." Longcope as a result of clinical observations was led to wonder whether nephritis might

Digitized by Google Original from HARVARD UNIVERSITY

not depend on a condition resembling protein intoxication. In experiments on animals to determine this, the marked cellular injuries in kidneys and liver following the injection of small quantities of protein "Suggest the possibility that in certain instances at least degenerative and cirrhotic processes in man may result from protein intoxication." (*Jour. A. M. A.*, April 18, 1914.)

The degenerative diseases apparently develop as a result of long continued intake of protein in excess of the quantity necessary to maintain nitrogen equilibrium and physical well being. This excess work so affects the process of metabolism that structural change follows — the kidneys, liver and cardiovascular system being involved with the greatest frequency. Acidosis and several of the diatheses are perhaps intermediate stages preceding well marked structural change.

Both from an economic standpoint and that of the relation to pathologic change the question of an essential lowering of the protein content of our dietary, is worthy of the earnest consideration of every medical man. In such questions the layman properly looks to the family physician for advice and through him only may positive results in health matters be expected.

POST-GRADUATE MEDICAL INSTRUCTION IN AMERICA

One of the results of the war of immediate interest to the medical profession in America is the changed condition with respect to post-graduate instruction in medicine.

The medical institutions of Europe, like its inns, were organized to accommodate all classes of students. Some well prepared men entered the universities, complied with the usual admission requirements, presented a satisfactory knowledge of the language of the country and became candidates for the higher degrees. On the other hand, a great army of general practitioners annually applied for post-graduate instruction who really desired "brush-up" courses. Owing to the deficiencies in their early undergraduate education they were attempting to receive "higher" education in subjects of which they were ignorant of the fundamentals.

The great medical centers of the United States, Philadelphia, New York, Baltimore, Boston and Chicago, meet the demands for our medical men in much better fashion than did Germany.

In the graduate departments of the great universities may be found opportunities for the qualified student for intensive work in the special fields of medicine and allied sciences under the tuition of men who have made a name in the world for American science and American methods; and in separately organized courses, a general review is offered to practitioners.

Contemporary Comment.

THYROID TOXEMIA AND EXOPHTHALMIC GOITER*

Exophthalmic goiter has long been ascribed to a condition of hyperthyroidism despite the difficulties of interpretation which this hypothesis entails. Toxic symptoms, even including exophthalmos, can be induced by ingestion of large quantities of thyroid extract. This well established fact is, perhaps, the most compelling indication for the hyperthyroid theory. Nevertheless, it has not sufficed to establish any acceptable or effective uniformity in the mode of treatment; and the dissatisfaction with the attempts to explain all the varied symptoms of exophthalmic goiter as the outcome of hyperactivity of the endocrine glands is manifested in current discussions of the pathogenesis and therapy of this malady.

Reviewing the criticisms of the theory of hyperthyroidism in relation to so-called exophthalmic goiter, Janney has reminded us that the typical exophthalmic goiter contains only from a fiftieth to a twentieth of the total active iodin present in normal thyroids; whereas more, not less, iodin might reasonably be expected to occur in hyperfunctioning glands. Exophthalmic goiter has been reported not infrequently in families having hyperthyroid members; sometimes both kinds of symptoms — supposedly hyperthyroid and hypothyroid — are observed in the same person. Contrary to the implications of the hyperthyroid theory, cases of exophthalmic goiter without tumor are not extremely uncommon. Despite the theory, thyroid medication has been reported to benefit some patients suffering from the disease. Finally, similar metabolic disturbances may be present in both alleged hyperthyroid and hypothyroid conditions; the blood picture of exophthalmic goiter is practically identical with that of myxedema and cretinism, so that, as Janney comments, if these conditions are diametrically opposed, such a striking similarity in the metabolic and hematologic findings would scarcely be expected.

Accordingly, Janney has proposed to discard the seemingly inadequate hyperthyroid explanation and substitute for it "dysfunction" of the thyroid to explain the phenomena. In the light of this we can now understand that some of the symptoms of exophthalmic goiter — the thyroid enlargement, cutaneous symptoms, scleroma, osseous changes, and special metabolic manifestations, such as hypoglycemia — are identical with those of a hypothyroidism attributable to a poorly functioning gland. They are truly symptoms of thyroid deficiency which have usually been disregarded in the symptomatology. The more familiar manifestations — psychic stimulation, tremor, tachycardia, increased basal metabolism, etc. — are

---

Jour. A. M. A., Dec. 14, 1918.

toxic symptoms which Janney assigns to the liberation of intermediate products of poisonous nature, perhaps owing to the incapacity of the glands to produce the normal thyroid hormone. In exophthalmic goiter, then, a toxic substance is circulating in the system. With a defective endocrine secretory function postulated, it becomes evident how hypothyroid and toxic symptoms may be discovered concomitantly.

With this tentative explanation it becomes clear, furthermore, how clinical improvement may follow suitable — not excessive — thyroid dosage in some cases, particularly when the thyroid deficiency is the etiologically prominent though perhaps not symptomatically conspicuous factor. It is also evident, on the other hand, that the introduction of a normal hormone from without to a dysfunctioning as well as underfunctioning endocrine organ "may not necessarily lead to a cessation of the chemopathologic processes causing the toxic symptoms" of exophthalmic goiter. Probably thyroid treatment of these toxic cases is inadvisable; but when the deficiency symptoms appear, thyroid therapy may actually be indicated, despite the objection which the still current hyperthyroid hypothesis interposes. Is it too much to expect that the stimulus of Janney's recently expressed views will lead to new clinical and therapeutic investigations untrammeled by the handicap of preconceived notions?

THE PREDETERMINATION OF SEX*

The old, old problem of the predetermination of sex, which has been a matter of much conjecture and hypothesis since, if not before, the days of Hippocrates, still remains an interesting one for solution. In a paper in the *Correspondenz-Blatt fur Schweizer Aerzte* for November 2, 1918, P. Scheurer discusses some of the theories that have been advanced and seems to favor the one that assumes the sex to be determined by the age of the ovum on the day of conception. His only real contribution in his analysis of Seigel's observations in 180 cases in which the date of the beginning of menstruation of the wife was known, and the exact date of the cohabitation was fixed through that of the soldier husband's brief furlough. It was observed that when, in these cases, the cohabitation took place during the first nine days after the beginning of menstruation, eighty per cent. of the children were boys; when it took place between the fifteenth and the twenty-third days after the beginning of menstruation eighty per cent. of the children were girls; when between the ninth and fifteenth days the number of boys and of girls were nearly equal. At first glance these figures seem to afford some support to the theory that the sex of the child is determined, to a large extent at least, by the age of the ovum on the day of conception, but a closer study shows that, aside from the fact that definite conclusions cannot be made from so small a number as 180 cases the evidence presented is inconclusive. The striking facts presented are that four-fifths of the children conceived during the days immediately following menstruation were boys, and that four-fifths of those conceived during the latter part of the intermenstrual period were girls, but in each case one-fifth of the children were of the opposite sex. Early age of the ovum failed to produce boys in one-fifth, late age to produce girls in the other fifth. The rule fails to work in one-fifth of the cases at each end of the scale. The exceptions in both the early and the late days are too numerous, even in this small number of cases, to permit the conclusion that the age of the ovum definitely predetermines the sex of the child. So far as Scheurer has proved anything, it would seem to be that the age of the ovum on the day of conception appears to have an influence on the predetermination of sex, and that other factors which are capable of over-riding its influence appear to exist. Inasmuch as the nature of these other factors remain unknown we seem to be as far as ever from a solution of the problem.

LOWERED RESISTANCE PAVES WAY FOR INFLUENZA*

An observant hospital corps man of the Navy became so thoroughly convinced that lowered resistance was always the determining factor in contracting influenza that he and some of his mates volunteered to test the truth of his theory. The offer was accepted and 100 enlisted men who volunteered were submitted to exhaustive experiments, by naval surgeons, the outcome of which seem to confirm the theory. These men were all in the best of physical condition, and during the experiment their health was looked after carefully. Live cultures of influenza bacilli were sprayed in their throats and noses hourly. The germs were introduced into their food. They were kept in close contact with patients suffering from the disease, and in order to obviate any possible individual immunity to one particular strain, the contacts were alternated frequently. Some members of the group received various preventive inoculations, but others were not thus protected. Not a single case of influenza was developed.

The size and condition of the thymus gland is an index of body nutrition at large. It supplies the excess of phosphorus needed by the body during early growth of the osseous system, the brain and nervous system.

The New York City Office of G. W. Carnrick Co. has removed to larger quarters, 13-15 Laight Street, one block south of old address.

---

* *N. Y. Med. Jour.*, Feb. 8, 1919.

* *N. Y. Med. Jour.*, Feb. 8, 1919.

DIET AND MILK SECRETION*

Not long after the demonstration that beri-beri is a disease attributable to a deficiency of the dietary came the announcement that the nursing infants of mothers who were suffering from the malady might also exhibit the symptoms. Judging from the ordinary chemical analysis there was no reason to assume that the milk furnished by the victims of beri-beri was deficient or unusual in its content of the ordinary nutrients. Fats, proteins, carbohydrate and mineral salts seemed to be present in the usual proportions. Soon it began to appear that milk is the carrier of something more than these familiar ingredients. Milk contains vitamins of more than one type. Evidently these may fail to be transmitted to the secretion under certain conditions of malnutrition in the lactating mother. Thus we are brought face to face with the unanticipated possibility that a product, milk, highly prized as an almost ideal food, may be of excellent quality as judged by the traditional standards of purity and value, and yet may lack something quite as essential as the calorie-yielding ingredients.

To what may the failure to produce perfect milk be charged? Does the synthetic capacity of the mammary gland fail in its duty, or is the production of nutritively imperfect milk associated with the diet of the lactating individual? The latter assumption seems somewhat unlikely in view of the now current doctrine that it is "breed" rather than "feed" which determines the character of the milk of any species. The mammary gland is not merely a filter which separates indiscriminately the varying pabulum brought to it by the blood stream. It seems to yield a product of almost invariable character despite profound alterations in the food intake of its bearer. This has been found to be true of cattle; and it was long ago reported that during the siege of Paris in 1870 young and vigorous women maintained and in some cases even induced gains in their suckling infants while these mothers themselves were actually or nearly starving.

Nevertheless, the synthetic powers of the mammary gland have evident limitations. Underfeeding and faulty diets are not without effect on the milk secretion; but it has remained for the more recent methods of biologic analysis — as it has been termed in contrast with ordinary chemical examination — to reveal the more subtle deficiencies that are the expression of the relation between improper food supply and milk production. The substantiated facts in this connection have recently been summarized by McCollum and Simmonds of the newly established School of Hygiene and Public Health at Johns Hopkins University, to whom are due fundamental researches in this field. The evidence, they state, seems conclusive that there is no special synthetic power of the mammary tissue by virtue of which amino-acids that are not found in the food can be formed. It is true that the milk contains proteins of uniquely good nutritive quality so that young animals may grow far better on a small concentration of these than on a much larger intake of plant proteins, for example. What happens, however, is this: The maternal organism selects certain of the amino-acids from the digestion products of the food and presents them in the milk incorporated in proteins in such proportions as make a very efficient transformation into the tissue proteins of the young. To quote McCollum and Simmonds, the mother "makes from her large intake of protein of rather poor quality a smaller output of protein of exceptional biologic value in the milk." This involves no synthesis of amino-acids de novo — only a selective absorption and reconstitution of the amino-acids which circulate in the blood, into complexes, the milk proteins, which in turn act as food that is very efficiently converted into body proteins for growth.

Similarly, according to McCollum, Simmonds and Pitz, the mammary gland picks up from the blood the as yet chemically unidentified vitamins and passes them into the milk. They cannot be produced synthetically, for when they are absent from the mother's diet the vitamins are not found in the milk. The demonstration of the production of an otherwise normal milk poor or lacking in the fat-soluble or water-soluble vitamin or both, and therefore not capable of inducing growth, is an item of great moment for the science of nutrition. It deserves to be emphasized prominently that "milk production may take place under dietary conditions such that the product is deficient in certain complexes necessary for growth." And it is a seemingly logical inference from this that deficiencies in the supply of certain inorganic nutrients to the mother may lead to consequent imperfections in the milk she secretes. The quality of milk needs to be evaluated from new standpoints.

Today we know that many of the items in the food supply of the less well to do may be poor in vitamins. Breads and other products prepared from highly milled cereals, refined sugar, vegetable fats, butter substitutes and meats belong to the staples in the rations of these people. Perhaps, therefore, there is no undue exaggeration in this contention of the Johns Hopkins bio-chemists:

> There are tens of thousands of human mothers who are attempting to nurse infants on diets derived too largely from the seeds of plants and their milled products. Such diets produce inferior milks and may be the cause of grave disorders in the very young.

The remedy lies in the suitable extension of the dietary, in the use of green vegetables and fruits, and the inclusion of milk as far as economic conditions and financial resources allow.

---

*Jour. A. M. A., Nov. 2, 1918.

Digitized by Google Original from HARVARD UNIVERSITY

THE FUNCTION OF THE ADRENAL CORTEX*

An article on the influence of the adrenal bodies upon the genital system, written by Dr. Swale Vincent, Professor of Physiology in the University of Manitoba, for a discussion at the American Gynaecological Society eighteen months ago, has recently been reprinted. It contains an interesting summary of the facts of comparative anatomy bearing upon the functions of the adrenal body. Dr. Vincent illustrates by diagrams the fact that the medulla and cortex belong to two different systems, and that their association in the adrenal body is, so to say, an anatomical accident. The medullary substance is an accumulation of the chromaphil tissue which has arisen from the sympathetic in certain abdominal segments and has insinuated itself into the adrenal body proper, that is, into what is usually called the cortex.

The adrenal cortex is developed from the germ epithelium, as are also the accessory cortical adrenals which occur so commonly in many animals as to compel us to regard the cortex as part of a system. His contention is, therefore, that it would be wise for investigators to search for a separate function for each of the two systems, cortex and medulla; there is already evidence strongly favoring the view that the cortex has certain important functions in connection with the development and growth of the sex organs. There is also abundant experimental evidence that it is the cortex, and not the medulla, which is essential to life. Extracts of the cortex do not contain any very special physiological principle. It is true that when injected into the veins of a living animal they lower the blood pressure, but this action is common to extracts made from all organs and tissue. The nature of the substance producing this effect is not certainly known; it is not choline, but it is possible that it may be betaiminazolylethylamine.

The cortical cells contain numerous lipoid granules, the so-called cortical granules; their function is not known, but it may be that they are to be regarded as secretions about to be poured into the blood stream. The function of the adrenal cortex has not been ascertained, but there is good clinical evidence that it is related to growth and development especially of the sexual organs. Bullock and Sequeira reported in 1905 that tumors or hypertrophies of the adrenal body were sometimes associated with precocious development of the reproductive organs.

Vincent adopts Glynn's classification of the tumors and rests of the adrenal cortex. The main divisions are into (a) diffuse hyperplasia passing into adenomata, frequently associated with female pseudohermaphroditism, and (b) malignant tumors, either sarcomata or hypernephromata or mesotheliomata. Hypernephromata of the adrenal body in children is much commoner in females than in males, and tends to increase the male primary and secondary characters at the expense of the female. Enlargement of the adrenal bodies occurs in some animals in the breeding season and in pregnancy, and Glynn has found some evidence of enlargement in pregnant women. Some experiments in which small doses of the gland substance were given to white rats in their food seemed to show that enlargement of the ovaries or testes, as the case might be, occurred; but the evidence on this head is incomplete. Vincent admits that it is hopeless at present to attempt any explanation of the precise manner or the essential mechanism of the influence of the adrenal cortex upon the reproductive organs. The adrenal organs may secrete a hormone which passes into the blood stream and so reaches the reproductive organs; or there may be more than one hormone. It is, he thinks, possible that the simple physiological conception of underaction or overaction of the various ductless glands, now held to account for the various pathological states observed, may have to be supplemented or superseded by a consideration of modified or deranged function.

The paper by Colonel McCarrison, I. M. S., contains a striking observation on concurrent hypertrophy of the adrenals and atrophy of the reproductive organs. It was made in the course of an elaborate and laborious investigation on the pathogenesis of disease due to deficiency of certain accessory food factors. In experiments on pigeons he found that the absence of these factors from the diet led to atrophy of all organs and tissues except the adrenals, and that the atrophy of the testes was extraordinarily great. The average weight of the testes per kilo of body weight in healthy adult pigeons was 4.643 grams, but in those receiving a diet from which accessory food factors were absent it was only 0.4015 grams. In the same animals the average weight of the adrenal bodies was 100.3 mg. and 139.5 mg. respectively. The atrophy of the central nervous system was slight. This, as is well known, is what occurs in inanition. McCarrison finds that in inanition there is also hypertrophy of the adrenals, but atrophy of other organs, the brain excepted. The change in the adrenal bodies seems to be a true hypertrophy, as there is a proportional increase in the adrenalin content.

There are other points in McCarrison's conclusions from his experiments, which will appeal to thoughtful members of the profession, especially those who take an interest in the nutrition of children; his observation that deficiency of certain accessory food factors opens the door to infections and parasitic agents may prove of far-reaching importance.

**British Medical Journal*, Feb. 15, 1919.

GLYCOSURIA IN ELDERLY PERSONS

The following interesting letter appeared in a recent issue of the British Medical Journal:

Sir: In his interesting article on the climacteric of life, in the Journal of January 18th, Dr. Guthrie Rankin supports the view that a moderate amount of sugar in the urine of elderly people need not cause alarm; it has, however, been my unfortunate experience to meet with a good many tragedies directly attributable to its acceptance. It is no doubt true that "many patients may live in comfort and do a fair amount of work over many years with sugar constantly in the urine," but it is equally true that many suffer from complications, such as neuritis, boils, eczema, gangrene, etc., and a considerable proportion eventually die of coma, as happened to the illustrative case (G. D.) quoted by Dr. Rankin. There appear to be at least two types of case, chemically and pathologically as well as clinically, and the difference depends largely on the sugar content of the blood. In my experience even a moderate excretion of sugar associated with hyperglycaemia always leads in the course of time to complications, whether the patient is old or young, whereas glycosuria unattended by an excess of sugar in the blood under test conditions is not likely to give rise to trouble or shorten life, especially if, as happens so often in elderly people, the reducing substance in the urine is not really a sugar but the ketonic acid I have described under the name of "pseudo-laevulose." Before coming to the conclusion that a "glycosuria" is of small moment, therefore it is advisable to make sure of the nature of the "sugar" and also to determine whether the blood sugar varies only within normal limits. When these points have been definitely ascertained the treatment can be adapted accordingly and a reliable prognosis offered.

Dr. Guthrie Rankin's experience of the modern method of treating diabetes seems to have been rather unfortunate, for I find that a recurrence of the glycosuria is exceptional and does not occur if the diet is correctly balanced as regards fat and protein, as well as carbohydrate, and the patient is properly trained in its use. I agree that elderly people do not stand starvation well, but as a rule actual fasting is not necessary to secure a normal blood sugar and a sugar-free urine if a carefully arranged system of dieting is followed. The secret of success is individualization of the treatment and education of the patient, so that he may follow his diet intelligently, and it is for lack of these precautions, and in consequence of a too rigid adherence to a set formula of treatment I am convinced, that some have the unhappy experience of being "again, and yet again, cleansed in the purgatorial fires," as Dr. Rankin picturesquely puts it. I am, etc.,

P. J. CAMMIDGE.

London, W., Jan. 20th.

Articles of Interest

THE PREVENTION AND TREATMENT OF DIABETIC COMA

By P. J. Cammidge, M. D., Lond.

* * * Clinical experience and many laboratory experiments have suggested that diabetic coma is the culminating point of an increasing acidosis, and one might therefore expect that therapeutic measures to counteract and control the acidosis would prevent the onset of coma and cure it should it have developed. The obvious treatment would be to make good the alkaline reserves of the body and ensure their being maintained at the normal level by the administration of alkalies by the mouth or, if need be, by intravenous injection. It is true that a certain degree of success has apparently attended this method of treatment, and there are even a few cases of diabetic coma on record where large doses of sodium bicarbonate saved the patient, at any rate temporarily, but on the whole the results of alkali therapy have been disappointing, and it can hardly be claimed that the death-rate has been materially improved by it. After all, it is only symptomatic treatment which does not touch the source of the trouble, the excessive formation of organic acids. Moreover, the attempt to control an acidosis with alkalies is not always free from danger and discomfort. Large doses of alkali, such as are often necessary, are apt to cause irritation of the gastro-intestinal tract and give rise to nausea and vomiting, especially if not administered in very dilute solution, and then the large amount of fluid may overburden the stomach and throw excessive work on the kidneys. When taken over long periods alkalies interfere with digestion, tend to deplete the body of necessary salts, particularly chlorides, and have a depressing effect on the heart if sodium salts are chiefly used. Finally, as Joslin has pointed out, it is possible that the administration of alkalies over long periods may set free acid bodies existing combined, quiescent, and harmless in the tissues, and so do harm, for the constant use of alkalies appears to promote the constant excretion of acid bodies. It is doubtful, therefore, whether the attempt to treat acidosis and prevent coma in diabetes with alkalies is sound practice, more especially as Allen's experiments have shown that in diabetic dogs no apparent prolongation of life results from keeping the alkaline reserve of the body normal with alkalies given intravenously or by the mouth.

A more satisfactory way of attacking the problem would be to prevent the formation of unoxidized acid products by limiting the material from which they are derived, and this is quite a feasible proposition, for the work of Rosenfeld, Hirschfeld, Magnus Levy, and others have shown that fat is the chief source of the acetone bodies and that it is from the fat of the food they are mainly derived. Recent work has proved that careful control of the fat intake in the diet is one of the most certain practical methods at present at our disposal for preventing acid intoxication and subsequent coma. By this means Joslin,[6] who was a pioneer in that aspect of the treatment of diabetes, has been able to reduce his death-rate through coma from an average of 64 per cent. to 44 per cent.

There seem to be two reasons why systematic control of the fat intake in diabetes has been hitherto neglected: (1) the very prevalent idea that diabetes is merely a defect of carbohydrate metabolism; and (2) the generally held doctrine that loss of weight by diabetics must be prevented at all cost. Experiments with diabetic animals and clinical observation have alike shown that both these ideas are erroneous. Diabetes is not a mere inability to assimilate glucose; from the first it is a defect in the metabolism of carbohydrate, protein, fat, and probably mineral substances as well, so that treatment directed to the control of the glycosuria alone deals with one aspect of the disease and overlooks what may be more serious but for a time, less evident defects in the chemistry of the body. The treatment from the commencement must be based on the hypothesis that we have to deal with a general failure of metabolism, and that while restriction of a single food principle, such as carbohydrate, may suppress the symptoms temporarily the progress of the diabetic process can only be prevented and complications, including coma, avoided by dealing with the condition as a whole.

Fat being the principal source of the unoxidized acid end-products giving rise to acidosis, control of the fat in the diet of a diabetic is obviously a matter for serious consideration from that point of view alone, but it is also important from another aspect. It would seem that the weakened metabolic functions of the diabetic are capable of dealing with only a definitely limited load, and that when this load is exceeded failure of the metabolic processes occurs. Consequently, although a reduction of the carbohydrate in the diet may stop the glycosuria, it will not prevent the disease progressing if the total intake of food is maintained by adding fat or protein. The metabolic functions will then still be over-taxed, and in spite of an apparent improvement the glycosuria will eventually return with increasing acidosis, etc., For a time the progress of the disease may again be stayed by lowering the carbohydrate intake, but so long as the total load of food is not reduced the downward progress of the disease will continue. In other words, the case will have the characters of a progressive diabetes with a steady fall in carbohydrate tolerance, a type one so frequently meets, especially in young people where an attempt is being made to keep up the weight by over-feeding with fat and protein. If, on the other hand, such patients are allowed to lose weight until the body mass is reduced to a level that can be maintained by a total load of food below what can be efficiently dealt with by their defective metabolic powers the apparently inevitable progress of the disease is checked, return of the glycosuria is prevented, and acidosis is avoided, or at least kept within narrow limits. It is true that patients treated in this way become thin, but it does not follow that they are less efficient muscularly, for, as Williams' experiments have shown,[7] and my own clinical experience confirms his results, muscular efficiency and weight are not synonymous. A thin patient feeding within his metabolic limits can do more, and is less easily tired, than one who is over-taxing his metabolic powers in an attempt to maintain a hypothetical weight for an individual of his size or who is over weight.

Regulation of the fat intake in diabetes undoubtedly places in our hands a most useful weapon for combating acidosis, and it appears probable that the death-rate from coma may be materially reduced thereby, especially when control is exercised from the earlier stages of the disease, but it does not necessarily follow that no other methods are available to reduce still further a mortality which is appallingly high.

It has been for so long the custom to accept acidosis and coma as cause and effect in diabetes that the possibility of the acidosis being an associated, and perhaps an incidental, phenomenon has not received the attention it deserves. The failure of alkali therapy to achieve the results expected of it has been one of the main stumbling blocks in the way of a general acceptance of the acid intoxication theory, and it has therefore been suggested by some that the ketonic acids and their salts induce coma, not in virtue of their acid properties, as that theory assumes, but in consequence of some specific toxic action they possess. But experiment has proved that these substances are not poisonous to normal animals in doses likely to be met with in practice. To meet this difficulty it has been claimed[8] that aceto-acetic acid and its salts are toxic if the animal is first rendered diabetic by extirpation of the pancreas. I am not prepared to deny that a diabetic and a normal animal may react differently to these substances, and that they may be more poisonous to the former than to the latter, but the fact that a condition which is known to alter fundamentally the metabolism of the body, and of itself leads to coma, has to be instituted before reasonable doses produce a toxic effect rather tends to weaken the force of the argument.

There can be no doubt that coma is the consequence of an auto-intoxication, but consideration of the evidence available suggests that it is a toxæmia resulting rather from the general failure of metabolism occurring in diabetes than from a specific toxin originating in a break in the chemistry of the body in one particular direction. It seems most likely that coma may be produced by several toxins of different origin acting together. In some instances, however, the metabolic defect may be more complete or rapid in one direction than another, and occasionally there may be associated defects in excretion, such as we know to occur in interstitial nephritis, which will cause one type of poison to have a preponderating effect. In this way we can account for the variations in the symptoms met with in different cases and for the occasional beneficial effects of the alkaline treatment.

---

[6] Treatment of Diabetes Mellitus, Lea and Febiger, 1917, p. 342.

[7] Arch. Int. Med., September, 1917, p. 399.

[8] Poulton: *The Lancet*, June 29th, 1918, p. 897.

Possible sources of toxins, other than fat, are carbohydrate and protein, while the modifying influence of inorganic salts on metabolism must also be taken into account. It is unlikely that carbohydrates give rise to poisonous materials that tend to produce coma directly, for experience has shown that increase in the carbohydrate content of the diet when coma threatens often brings about a temporary improvement, especially when the patient has been treated previously on the historic lines of a "carbohydrate-free" diet, consisting chiefly of protein and fat. Indirectly an excess of carbohydrate in the diet, no doubt, has an influence in causing this complication, first through its effect in accentuating the metabolic deficiencies which underlie the diabetic condition, and secondly through the dehydration of the tissues consequent on the presence of an excess of sugar in the circulation. Water is needed to maintain the volume of the blood required for the mechanical efficiency of the circulatory apparatus, to carry nourishment to the cells, to remove the waste products of metabolism in solution, and to maintain the osmotic conditions essential for cell life. When it is abstracted from the body, and the loss is not made good owing to conditions of the gastro-intestinal tract which prevent retention and absorption, acidosis, sudden large inflammatory exudates, and other reasons, serious and rapid loss of weight occurs, the respirations and pulse increase in frequency, the systolic blood pressure falls, the tension of the eyeball is markedly diminished, the tongue becomes dry and parched, there is oliguria with constipation, the patient becomes restless and irritable, then apathetic, and, finally, comatose. The similarity of these symptoms to many of those met with during the onset of diabetic coma suggests that some of the latter, at least, may be a consequence of the dehydration of the tissues produced by a high concentration of sugar in the blood. It also helps to explain the frequency with which coma is precipitated by gastro-intestinal disturbances, particularly when there is vomiting or diarrhœa, and by conditions where large inflammatory exudates take place.

* * * It has been shown experimentally that some of the products of protein disintegration are toxic, producing among other symptoms lowering of the blood pressure, depression, and narcosis, but no attempt appears to have been made to isolate such substances in diabetes. Some experiments I commenced four or five years ago with that end in view had to be abandoned temporarily, but so far as they went, and taken in conjunction with the results of the routine analysis of the urine in a large number of cases, they showed that protein metabolism in diabetes tends to become less and less complete as the disease advances, and that this is associated with a progressive failure in the functions of the liver similar to what is met with in acute yellow atrophy, some of the toxæmias of pregnancy, etc. One of the most striking features of the urine in all severe cases of diabetes is the constant presence of amino-acids, which increase in amount as the disease advances, so that the amino-acid nitrogen often constitutes 50 per cent. or more of the total "ammonia nitrogen" as estimated by the Malfutti formalin process. In one instance, for example, I found 6.3 g. of amino-acid nitrogen out of a total of 7.8 g. of "total ammonia nitrogen" in a 24 hours' specimen of urine passed six days before death from coma took place. In three cases where an analysis of the collected 24 hours' urine was made shortly after the premonitory symptoms of coma had appeared the amino-acid nitrogen was found to have dropped suddenly and in one had entirely disappeared, although 4.3 g. had been present the previous week. The nature of the amino-acids was investigated in 11 cases, three of which eventually died of coma. Tyrosin, histidin, phenyl-alanin, and glycocoll were found in all, while tryptophan, alanin, leucin, and arginin were only met with in the more advanced. In two cases, both of which died shortly after of coma, an amine resembling in some respects a toxic base described by Dale and Laidlaw[9] was isolated. Very often a marked increase in the uric acid output, which may reach 8 or 9 g. a day, is seen at, or about, the same time as the rise in the amino-acid nitrogen occurs and without any change in the diet being made. As a rule, the curves of excretion of uric acid and creatinin tend to run in opposite directions in diabetes and the rise in the uric acid preceding the onset of the symptoms of coma is no exception, a corresponding fall in the creatinin output usually being seen. Simultaneously the excretion of urobilin in the urine increases. These observations point to the onset of coma being associated with a failure in the functional activity of the liver, and it seems likely that the resulting imperfections in protein metabolism may be a contributory factor at least in bringing about the condition.

In a previous paper[10] I considered the effect of the withdrawal of bases from the tissues resulting from acidosis, and particularly of calcium and magnesium. I there pointed out that a balance between the two appears to be necessary for the smooth and efficient working of the nervous

[9] Journ. Physiol., 1910, xli., 318.

[10] American Medicine, June, 1916, p. 370.

system and that an excessive loss of magnesium is associated with nervous instability. A striking increase in the magnesium and calcium loss in the urine is a constant feature of all severe cases of diabetes, and it is not unlikely that this loss renders the nervous system more susceptible to the action of toxins formed in the liver and elsewhere. The experiments of Osborne, Mendel, and Ferry lend support to this view, for they found that rats fed on a diet poor in inorganic salts, but otherwise satisfactory, eventually developed coma, and that they could be resuscitated by the administration of a mixture containing calcium and potassium phosphate, sodium chloride, and citrates of sodium, iron, calcium, and magnesium.[11]

If, as the foregoing considerations suggest, diabetic coma is not due to one cause, but is a complication arising from the cumulative effects of several, which result from the general metabolic failure of the diabetic organism, it is clear that treatment directed to one cause is not likely to control the symptoms, at any rate, more than temporarily, and that the only "cure" is to prevent all possible causes by so arranging the diet that (1) the patient's tolerance for carbohydrate, protein, and fat is not exceeded; (2) the total load of food is within his metabolic capacity; (3) the diet is correctly balanced; and (4) a sufficient allowance of inorganic salts is provided. Obviously the earlier in the course of the disease such treatment is commenced the better are the results likely to be and the less difficult will it prove to arrange a diet fulfilling the necessary conditions, but even with advanced cases a surprising improvement can be effected by careful dieting along these lines.

When a diabetic patient is first seen no change should be made in the character of his food. If possible he should be kept for a few days on an ordinary mixed diet of known composition and the opportunity taken to investigate his metabolism by analyses of the urine, blood, etc. The effect of excluding fat from the diet should then be tried. After a day or two on a fat-free diet the protein may be reduced by half. Subsequently the carbohydrate allowance may also be halved, then the remainder of the protein excluded, and the carbohydrate further reduced until a diet of green vegetables of low carbohydrate value only is being taken. If sugar is still being excreted in the urine or the blood sugar is high and serious acidosis or evidence of abnormal tissue waste persist, two or three days' "starvation" may be prescribed, but longer continuous fasts are best avoided. Abstinence from food usually has a remarkable effect, improving carbohydrate tolerance, correcting errors in protein metabolism, and reducing acidosis, so that patients apparently in a grave condition may often be rescued and put on a metabolic basis that permits of a satisfactory diet being subsequently constructed.

The building up of the diet must be gradual and be carried out in the reverse order to that outlined above — that is to say, green vegetables alone, with a gradually increasing carbohydrate content, should be allowed first, then a very limited amount of fat-free protein, such as boiled white fish or chicken, is added, more carbohydrate is next given, and later the protein is increased until the patient is in nitrogenous equilibrium. When this point is reached fat may be allowed, at first in small quantities and later in larger amounts, but the effect on protein metabolism and the utilization of carbohydrate must be carefully watched by regular examinations of the urine and blood. It is necessary that part of the carbohydrate should continue to be taken in the form of green vegetables, the exact proportion varying according to the patient's tolerance for starchy foods. It is also an advantage if at least one serving of raw vegetable (e. g., as salad) is eaten each day. These precautions not only help to overcome the constipation from which most diabetics suffer, but also ensure a sufficient supply of the inorganic bases that are essential for proper metabolism and render the medicinal use of alkalies unnecessary.

No attempt should be made to work the diet up to a theoretical caloric content based upon the size of the individual. If this can be done without risk so much the better, but the future progress of the case should not be sacrificed for a merely temporary benefit. The diet must be arranged to suit the patient's present metabolic capacity, not his appetite; in other words, he must be taught "to eat in order to live, not live to eat." The cardinal and very common mistake of an unbalanced diet should be carefully avoided. The effect of an excess of carbohydrate soon shows itself in the urine and is easy to recognize, but the equally deleterious results of too much protein or fat are not at once so evident. The best guide to the protein limit is the nitrogen balance, and the protein allowance should be so arranged that its nitrogen content does not exceed the daily total nitrogen output in the urine by more than 1 or 2 g. So long as this ratio exists further trouble from disturbances of protein metabolism need not be feared. Fat, unbalanced by other foods, is an insidious poison for the diabetic, and every endeavor should therefore be made to keep the fat allowance at a level corresponding to the patient's capacity for dealing efficiently with other foods. For practical purposes it may be taken that the allowance of fat, at least in the earlier stages of treatment, should not exceed the allowance of carbohydrate, or at most not be more than half as much again. A higher proportion is likely to lead to subsequent difficulties, and these are certain to occur if the proportion of fat to carbohydrate is more than 4 to 1. Determination of the fat content of the blood is undoubtedly the best guide for ascertaining the optimum allowance of fat in the diet, but regular estimations of the percentage of sugar in the blood also give useful indications, for a steady increase, especially if not associated with glycosuria, suggests that too much fat is being taken.

---

[11] Carnegie Institute of Washington, 1911, 156, ii., 80.

I have recently had under my care a patient, sent to me by Sir John Tweedy owing to an eye trouble associated with diabetes, who illustrated this point very well. When I first saw him his blood sugar stood at 0.20 per cent. and he was passing 15 g. of sugar a day in his urine. After a week of treatment the glycosuria had disappeared and his blood sugar had dropped to 0.08 per cent. A week later on a diet containing 50 g. of carbohydrate and 70 g. of protein, but practically no fat, the blood sugar had risen to 0.11 per cent. He was then given fat in gradually increasing amounts up to 60 g., when it was found that the blood sugar had risen to 0.18 per cent., although there was no sugar in the urine. On dropping the fat to 10 g. but not otherwise altering the diet, the blood sugar came down to 0.11 per cent. again. A return to the previous allowance of fat was followed by a rise in the blood sugar to 0.18 per cent., but still without glycosuria. * * *

—*The Lancet*, January 11, 1919.

SPANISH INFLUENZA

BENEFICIAL RESULTS OF CONTINUOUS STIMULATION OF THE HEPATIC DETOXIFYING FUNCTION BY MILD DOSES OF CALOMEL*

W. L. Mann, Ph. B., A. M., M. D.,
Lt. Comdr. U. S. Navy. Marine Barracks, Quantico, Va.

This article is written under the assumption that calomel acts as an hepatic stimulant. Its mode of action and the correctness of this assumption are beyond the scope of this paper. Notwithstanding the results of experimentation, it appears to be the consensus of opinion among practising physicians, especially those with tropical or sub-tropical experience, that calomel exerts a certain hepatic influence.—
— W. L. M.

The pendulum of professional, as well as public, opinion presents a tendency to vary from one extreme to the other. This is especially true of therapy in certain diseases.

During the recent epidemic of influenza, with its sequela, pneumonia, the medical department of this Post had an opportunity to use as a routine measure one of the well-known remedies with gratifying results.

It has been the experience of the writer that recent graduates in medicine have been reluctant about the use of calomel, and have relied principally on oils and saline laxatives. The older school of medicine has probably gone to the other extreme, and has given such large doses of this medicine, on occasions when it was not required, that it is possible that this is explanatory of the fact that the pendulum of professional opinion has now appeared to have swung to the present extreme of conservatism.

During the above mentioned epidemic some rather striking results were obtained from calomel therapy on a few cases that were indirectly under my supervision. This was at first regarded as, perhaps, a coincidence.

After observing over three thousand cases of the so-called "Spanish Influenza," it appears to me that the disease is essentially a toxemia. Some of the cases considered as pneumonia appear to be more of a pulmonary congestion and edema, with expectoration of blood-tinged mucus; although there were many cases of purulent expectoration where typical symptoms of lobar or lobular pneumonia were noticed.

Detoxication is one of the many functions of the hepatic gland. For example, it appears that a larger amount of certain toxins may be injected into the portal vein than into the hepatic vein without fatal results. This is assumed to be due to the detoxifying action of the liver.

Acting on the assumption that the toxemia might be combated to some extent by stimulation of the hepatic function by mild doses of calomel, the following procedure was eventually adopted as a routine: (1) Calomel gr. 1/4 given every half hour for six or eight doses, followed by a mild dose of magnesium sulphate in the morning, or preferably, if patient was very ill, an enema was substituted. (2) Calomel gr. 1/10 was then given four times a day for three or four days.

The above routine was made flexible and elastic so as to permit individualization of treatment. In many cases where the fever tended to show secondary rises, or to remain high, the administration of two grains of calomel in fractional doses was repeated with rather good results.

In some cases nausea may be caused by these fractional doses of calomel and, if so, it should be discontinued temporarily, although in many cases nausea and vomiting was one of the pronounced symptoms of the disease.

The routine use of calomel was not adopted until the fourteenth day of the epidemic, therefore the presentation of any statistics on the mortality rate before and after its adoption might lead to fallacious deductions, as there are other factors which enter into consideration.

It will suffice to state that the wards which first adopted this treatment presented a much better appearance and a lower mortality rate than the other wards. Also, since the adoption of this therapy as a routine, the ward medical officers are unanimous in their opinion that beneficial action has resulted from its use; however, their individual opinions, as to be expected, show varying degrees of enthusiasm about its success.

Notwithstanding the apparent beneficial action of this treatment, the total number of fatalities

---

**Medical Record*, February 8, 1919.

from this disease on this station is rather disappointing; however, the indications are that the case fatality rate will probably compare favorably with other places.

The best results were obtained in the early treatment of cases by this method. The cases of influenza that had progressed for some days failed to respond to calomel as readily as the incipient cases.

Of course, it is assumed that other remedies will be used in conjunction with this therapy.

Summary and Conclusions.— 1. The influenza cases treated with an initial calomel purge followed by 1/10 gr. calomel, four times a day, presented less toxic symptoms, nausea was not so pronounced in many of the cases, and the mortality rate was not so high.

2. The beneficial results were rather striking, although no specific action is claimed.

(This judicially written article is deserving of commendation. There is no doubt that calomel by its action on the liver and its subsequent effect upon the intestinal tract by increased discharge of bile with relief of constipation resulting from the biliary insufficiency, is deserving of a place in the treatment of such a condition as "Spanish Influenza."

However, there is another phase to the therapeutic situation. It is well known that small doses of mercury have a stimulating effect upon the glands of internal secretion, especially the thyroid and suprarenals, which are especially concerned in combating the toxins of such a disease.

Sajous has given a graphic illustration of this (*Endocrinology*, Vol. 1., No. 1., page 9). He says: "On a Mediterranean-transatlantic liner, some years ago, diphtheria reigned supreme in the sense that the antitoxin on board seemed to have lost its efficiency — owing probably to deficient reactive powers on the part of the obviously debilitated immigrant children affected. Night after night a child or two were buried at sea. In despair the ship surgeon sought our aid, and we suggested that calomel be given orally besides the injections of antitoxin. The burials promptly ceased. The ductless glands had reacted and poured into the ~~blood~~ autoantitoxin which, added to the exogenous antitoxin injected, won the day."

Sajous takes care, however, to discriminate between the use of small doses of calomel and the effect following the use of large doses of the same medicament. He points out that in large doses it has a pernicious influence on these glands.

It is well worth while to point out these things, because, while in most cases the use of calomel is followed by very obvious results, the subtleties of the therapeutic situation are apt to be overlooked.— Ed. METABOLIST.)

THE CORRELATION OF THE INTERNAL SECRETIONS IN REGARD TO THEIR GENITAL FUNCTIONS*

BY W. BLAIR BELL, B. S., M. D., LOND.

I have endeavored to trace, for the most part from my own observations, the disjointed facts concerning the influences exerted by the different members of the endocrinic gland system upon one another, on the genital organs and on the metabolism generally, in so far as the reproductive system may be concerned; and in so doing I have in some cases been able to show clearly the nature of the associations between the different organs. It is, however, absolutely impossible at the present time fully to correlate all their functions; but in view of what was said at the commencement as to the necessity for a lead in this intricate matter, I cannot refrain from enunciating what I believe to be the general principles. I shall not further analyze the details.

It appears, from the evidence at our disposal, that in spite of great variations in the structure of the endocrinic glands in different mammals, the *total functional result* is the same so far as the genital processes are concerned. The variations in function that depend on the differences of structure, are probably related to differences in the food and habits of life; and in adapting our knowledge to the requirements of human physiology we must take into account both the essential functions to which we have already referred — the individual metabolism of the mother, and the metabolism of her reproductive functions — for they are completely interdependent in normal circumstances.

We have seen as the result of our studies that the ovaries, on the one hand, have as their share of these dual functions the onus of ensuring the reproduction of the species by furnishing the ova, and by keeping active the rest of the genital structures and functions. And, further, the secretions of the ovary are probably concerned in keeping the other members of the endocrinic system in touch with the necessities of the reproductive situation. This last function is of the deepest importance, and is one which explains much that would otherwise be obscure.

Strictly speaking, then, the ovary, is concerned in the temporary function of reproducing the species, and, by its hormones or internal secretions, of bending the metabolism of the body to this purpose. Any influence the ovary may have over the general metabolism, is, then, related to and dependent on its primary reproductive functions. I do not believe that this organ influences the metabolism except in so far as this special function is concerned. Of course, removal of the ovaries may produce a temporary general disturbance, but this does not invalidate the view just mentioned.

---

* *The Sex Complex*, p. 97.

On the other hand, the rest of the endocrinic system is related to the genital functions in various ways. First, some of the members — the thyroid, pituitary, and suprarenals — influence the development and subsequently preserve the integrity and activity of the genitalia, as I have already demonstrated; while others — the thymus and possibly the pineal — appear to prevent sexual precocity. Second, all the endocrinic organs, acting in harmony, control the metabolism in response to the necessities of the genital functions; but, in addition, they adapt the whole organism to the possibility of the situation, and regulate the secondary characteristics, both physical and psychical, to suit the needs of the individual. Once, however, the reproductive organs are removed or undergo atrophy, the genital functions of the rest of the endocrinic system cease, and the rearrangement of the metabolism that follows produces the symptoms of the menopause, as we shall see later. Contrariwise, insufficiency of the thyroid, pituitary or suprarenals may cause the cessation of the genital functions with atrophy of the uterus.

As to the more particular parts played in the metabolism by each member of the ductless gland system, these have already been specified.

In spite, therefore, of the reluctance to correlate our knowledge shown by most investigators the matter is not one of very great complexity if the views expressed be correct in a general way, although there remains much detail to be filled in.

As soon as possible we must come to a conclusion as to what are the facts; so much of the work that has been done is contradictory. There is in consequence so much more need for further efforts. And I would again insist that in order completely to solve the problems surrounding the genital functions, we must focus at one and the same time the two essential processes of life — the individual metabolism and the reproductive metabolism. They are absolutely interdependent; indeed, the individual metabolism is the reproductive metabolism. It is the neglect of this point of view that has brought about much of the confusion that still exists.

Weismann and Ray Lankester describe the relation between the reproductive cells and those of the soma in still more striking terms. The latter says: "Among the multicellular animals, certain cells are separated from the rest of the constituent units of the body, as egg cells and sperm-cells; these conjugate and continue to live, whilst the remaining cells, the mere carriers as it were of the immortal reproductive cells, die and disintegrate. The bodies of the higher animals which die may from this point of view be regarded as something temporary and non-essential destined merely to carry for a time, to nurse and to nourish the more important and deathless fission products of the unicellular egg."

Whatever views we may hold as to details I question whether this philosophical statement is open to contradiction. The function of reproduction in all its preparations and performances commences in the early stages of segmentation, and may be said to continue in Man until the care of the offspring is completed; but in many lower forms of life, male and female, the act of reproduction is also the cause of death.

A BRIEF STUDY OF GOITER*

E. P. Sloan, M. D.

The greatest difficulty in the scientific study of goiter in its various phases and relations is the absence of standard nomenclature. Even a definition that really defines goiter has not been proposed. The old-time definition "An enlargement of the neck," even though modified by the phrase "Due to enlargement of the thyroid," is incorrect and unsatisfactory. Over fifty per cent. of the patients that we have seen with real exophthalmic goiter have had no enlargement of the neck. The most satisfactory definition that I can suggest is "A goiter is the diseased portion of a thyroid gland."

There is no classification for goiter that is standard. It seems that every goiter investigator adds to the already uselessly large number of divisions and classifications. This is perhaps due to the fact that the pathological classification bears so little relation to the clinical picture. The size of the goiter has small relation to its pathological classification or to its clinical picture. The exophthalmus may be the remaining symptom of an old hyperthyroidism that has long since changed into a hypothyroidism with destructive degeneration of the gland.

The symptoms of a case vary. At the first they may be due to acute hyperthyroidism, later to hypothyroidism and at last to thyrotoxis and pressure symptoms. A patient may have had almost every known symptom and conformed to almost every known classification.

We have used the following classification:

Simple goiter or an enlargement of the gland with no active systemic symptoms.

Hyperthyroidism.

Hypothyroidism and Mixed.

A TASK!

To be honest, to be kind; to earn a little and to spend a little less; to make upon the whole a family happier for his presence; to renounce when that shall be necessary and not to be embittered; to keep a few friends, but these without capitulation; above all, on the same grim condition, to keep friends with himself, here is a task for all that man has of fortitude and delicacy.

Robert Louis Stevenson.

---

* *Illinois Medical Journal*, May, 1919.

Brief Abstracts

Observation on Three Cases of Scurvy.—VILHJALMUR STEFANSSON (*Journal of the American Medical Association*, November 23, 1918.)

Stefansson reviews the experience of seventeen members of the Canadian Arctic Expedition in the winter of 1916-1917. Groups of men taking large quantities of canned and salty food and little fresh meat on the one hand, and those taking large quantities of fresh meat on the other, presented an unusual opportunity to study the effects of such diet on the development of scurvy. Scurvy did not develop among those eating fresh meat and three well-developed cases occurred among those who did not. All cases of scurvy were cured by eating either putrid uncooked meat or cooked unsalted fresh meat. The results in every case were positive and took place in a very short time — two weeks to one month.

Stefansson's conclusions are:

1. The strongest antiscorbutic qualities reside in certain fresh foods and diminish or disappear with storage by any of the common methods of preservation — canning, pickling, drying, etc. Fresh tomatoes may be valuable (I have never tried them), but canned tomatoes are of little or no value; fresh potatoes are good, but desiccated potatoes have shown little or no adequacy in our expedition when tried in my absence by believers in that form of diet; the juice just expressed from the fresh lime is said to be excellent and I have no reason to doubt it; but bottled lime juice has never yet prevented scurvy. (I have just recently gathered interesting but scarcely needed testimony on this point from the Royal N. W. Mounted Police as to the scurvy winter of 1898-1899 at Dawson.)

2. Cooking lessens or destroys the anti-scorbutic value of most or all foods. Three average raw potatoes are commonly said by miners definitely to turn the tide of scurvy that has not reached an extreme stage; in our own expedition, boiled and roasted fresh bear meat did not relieve scurvy except with such slowness that it is debatable just what its effect was, if any. Our party and persons known to me have had the same experience with venison. I am of the opinion that most men, if left to their own inclinations and supplied with abundant cooked, fresh meat will avoid scurvy; cooked meat acts but slowly on an advanced case — the efficiency of it depending probably on the "rareness" of the cooked meat.

3. Meat and fish slightly or well advanced in the process of ordinary putrefaction seems to be as good an antiscorbutic as fresh flesh, or nearly so — witness Andersen's case above and the well-known fact that Eskimo tribes often live for several months in succession on putrid meat or fish without ever developing scurvy, while Eskimos working for white men or living on purchased provisions have it quite as readily as Europeans living on the same sort of diet.

4. Bodily cleanliness and ventilation are not by any facts known to me shown to have any bearing on the incidence or severity of scurvy. Here it is instructive to compare the filth and good health of Nansen and Johansen, as described in "Farthest North," with the immaculate Scott expeditions with their numerous and serious scurvy cases.

5. Exercise does not prevent scurvy. I have been told, verbally, that the Scott party had it on the return from the pole, after months of continuous and strenuous work in the purest of pure air and in abundant, continuous sunshine; while Nansen and Johansen were in perfect health after a winter of the most nearly absolute inactivity ever known to me to have been described in a book of travel. These are not isolated but typical instances.

6. Salt, while not proved by anything I know to be a cause of scurvy, probably has some direct bearing on the history of the disease, for the following reasons: (a) Salt meats have long been recognized (and probably rightly) as pre-disposing to scurvy. (b) Many observers have commented on the hankering for salt by scurvy patients and on the disappearance of the longing as the cure proceeds.

Neither am I certain that salt did not co-operate with the heat in lessening the anti-scorbutic value of the meat used by four of our eight scurvy patients. The only death and the only long and dragging recoveries were of men who ate their meat cooked and salted during or after cooking. This was at the winter camps, which, while they belonged to our expedition, were not at the time under my personal observance, and I have the stories on hearsay.

7. It is a mistake to think (with most laymen and many physicians) that blackening of the skin of the leg and softening of the calf muscles are among the early symptoms in nearly all cases. I have never seen either symptom, and in the cases I have heard of from reliable observers these symptoms, if they appeared, appeared late in the disease. Dizziness on standing up and bleeding from the gums are commonly among the earliest symptoms noted by the sick man himself, though it may be right that careful tests would disclose other symptoms earlier.

Observations on the Cause of Rickets.—D. Noel Daton, Leonard Findlay, and Alexander Watson (*British Medical Journal*, December 7, 1918).

The authors made their investigations during the course of some experiments designed to produce experimental rickets in dogs in order to secure rachitic animals and normal controls for a study of calcium metabolism.

Former observation in this laboratory (Physiological Laboratory, University of Glasgow), had shown that rickets may almost certainly be developed in certain breeds of dogs by merely keeping the animals confined. Two litters comprising seventeen dogs were used.

Three dogs of the first litter were sent to the country and given plenty of out-door exercise — they returned to the laboratory in good health and on necropsy showed no sign of rickets.

Two dogs of the second litter sent to the country under the same conditions as the first, returned to the laboratory without any evidence of rickets. All five animals were fed upon oatmeal porridge and skimmed milk. It is estimated that not more than 2.8 grams of fat per day for each pup was contained in their diet.

Five pups of the first litter were confined in the laboratory. They were fed upon oatmeal porridge and whole milk — an estimated fat content per pup of from 3 to 6 grams per day. All showed marked rachitic changes by X-ray examination during life and at necropsy.

The remaining seven of the second litter were kept in the laboratory. Ten grams of butter were given daily to three of them. The food was the same as that of the first litter. Those without butter received from 3 to 6 grams of fat per day and those with butter 14.5 grams. All those kept in the laboratory showed signs of rickets to a greater or less degree. One which had been confined and had butter was most markedly affected. One which was confined and had no butter was least affected. All of those confined showed marked splaying of the fore feet, distinct rachitic changes of the wrist joints and softening of the femur.

There is no support for the theory of Funk that rickets may be due to the absence of some "vitamine," or of that of Bland-Sutton that rickets may be prevented by the administration of fats.

They conclude that:

1. "Pups kept in the country and freely exercised in the open air, although they had actually a smaller amount of milk fat than those kept in the laboratory remained free of rickets while animals kept in the laboratory all became rickety. The observations seemed to show that some other factor than diet is the prime cause of rickets in dogs and afford no evidence that milk fat (butter) contains any accessory factor protecting against the development of rickets."

The most potent factor in arteriosclerosis is overfeeding. The most universal factor is gastro-intestinal autointoxication.

Pituitary Headaches and Their Cure.— Irving H. Pardee (*Archives of Internal Medicine*, Vol. 23, No. 2, February 15, 1919).

Headache is a symptom of such a diversity of diseases that the patient who complains of it is too often given a cathartic and aspirin and dismissed without adequate study to determine its true etiology. It may occur in circulatory disturbance, hypertension, nephritis, anemia, acute febrile disease, toxic poisoning, syphilis, myositis of the occipito-frontalis, cranial gumma, inflammation of the accessory sinuses, abscess meningitis, tumor, errors of refraction, neuroses, psychoses, hysteria and from reflex causes.

The part which the pituitary gland may play in the production of headache is frequently overlooked. The syndrome caused by pituitary tumors is well known — severe frontal headache, somnolence, mental dulness, polyuria, increased sugar tolerance or glycosuria, oculo-motor palsies, bitemporal hemianopsia, evidence of disturbed bony metabolism or adiposity, sexual regression, etc., but the early and not so easily recognizable pituitary disturbances should be studied.

One of the first symptoms of a pituitary gland which is functioning improperly is a frontal headache which does not yield to the usual remedies.

The cause of pituitary headaches is an enlargement of the hypophysis following a stimulus or demand made on it, or a pathologic condition of the gland. It is more common in women and is seen most frequently in adolescence or early adult life.

The anatomical relations of the hypophysis are such that, surrounded on three sides by bony structure, a very slight enlargement will bring about a train of symptoms dependent upon this mechanical discrepancy. Comparative measurements of the normal hypophysis and the bony bed in which it lies, the sella-turcica, indicate that the normal gland has a normal sella formation, but should the glandular function be disturbed there will result certain signs and symptoms and the roentgenogram will show an abnormal sella-turcica.

Roentgenograms of cases of "pituitary" headache and dyspituitary signs reveal marked changes in the sella and form a valuable diagnostic procedure. Pituitary enlargement may take place at menstruation, pregnancy and from other glandular disturbances, pineal, thymus, adrenal or thyroid.

The pituitary headache has three characteristics: its location; its duration and persistence; and its relief under specific medication. Marked fatigue occurs and the white line (Sergent's) of suprarenal insufficiency may be demonstrated. Disturbances of sugar metabolism may occur. The growth of hair is apt to be dark and coarse and abundant. The eyebrows are heavy and long and often meet in the middle line. The female may show a tendency to a mustache. The bony framework may be altered. The administration of pituitary extract is specific in the treatment of pituitary headaches, ¼ to 2 grains three times a day. After the symptoms show improvement the dose should be diminished.

Conclusions:

1. Pituitary disturbances constitute a fairly common cause of headache.

2. Pituitary headache is located between the temples, deep in behind the eyes and is accompanied by dyspituitary signs.

3. Abnormality of the sella-turcica is demonstrable in almost every case of pituitary disease.

4. Administration of the whole gland cures these headaches and the accompanying symptoms in a large percentage of cases, provided there is not a progressive neoplastic growth.

Saline Solution with Organ Extracts in Shock.—Descomps and Clermonthe (*Presse Medicale*, August 22, 1918). Thirteen cases of shock hemorrhagic or toxic were treated within from 6 to 24 hours after injury, by intravenous injection of a hypertonic solution of about the same composition as Ringer's solution — to which was added a few mils of soluble extracts of thyroid, hypophysis, adrenals, testicles and spleen and a little strychnine and digitalin. This was administered to supply the temporary deficiency in the blood of the secretions of the endocrine glands, which exert a controlling action on the functional activity of the sympathetic and maintain the action of the váso-motor centres. Circulatory disturbances are a conspicuous feature of all shock.

Eight of the patients thus treated recovered and in five the measure was a failure.

The successful cases showed a regular and forcible pulse within six or eight hours. Blood pressure rapidly increased. Persistent diuresis and increased daily elimination of urea were noted. Urea output increased above the average to twenty-nine up to forty-two grams, suggesting an action on the liver. Chlorides were low. The specific gravity of the urine was always normal or above.

In some cases there was a diminishing of delirium, restlessness and mental disturbances.

The Milder Forms of Manic-Depressive Psychoses and the Manic-Depressive Constitution or Temperament.— B. Onuf (Onufrowicz), M. D. (*Medical Record*, Dec. 7, 1918).

The term manic-depressive insanity introduced by Kraepelin has unified and shown the common binding traits among such conditions as simple mania, melancholia, recurrent mania and melancholia, periodic mania and melancholia, circular insanity and the milder form cyclothymia. Kraepelin showed in persons showing alternating periods of mania and melancholia there is much more frequently than is generally believed a blending of these two opposite conditions. The following are typical phases.

1. Manic, depressive, and normal states may follow each other in regular succession in a typical cycle.— Circular or cyclic insanity, called cyclothymia in the mild form.

2. The normal state may be broken into by manic attacks and by depressive, *i.e.*, melancholic attacks at irregular intervals and in irregular succession.— Periodic manic-depressive insanity.

3. Manic attacks interrupt the normal state at various intervals, but they are rarely if ever purely manic; depressive episodes of longer or shorter duration, sometimes only of hours or less, sometimes of days, occur during the manic attack, or the manic attack is ushered in by a depressive forestage.— Periodic or recurrent mania.

4. Depressive or melancholic attacks interrupt the normal state at varying intervals, being again often or usually mixed with or preceded by manic episodes.— Periodic or recurrent melancholia.

5. Only one or two actual *manic* attacks occur in a lifetime, but the manic-depressive make-up to be described later is present.

6. Only one or two *depressive* attacks occur in a lifetime, but the manic-depressive make-up exists.

7. All other possible mixtures or combinations are found: A melancholic emotional attitude, for instance, may be associated with verbosity, flight of ideas; or a manic emotional attitude may be associated with a stuporous state.— Manic stupor.

It is not the purpose of this paper to dwell on the severe forms of mania and melancholia. I shall therefore refer to these briefly, not more than is needed for a general understanding of this subject.

In the marked manic attack there is exaltation, boisterousness, sense of increased power and verbosity, increased sexual desire. Activity is increased in a more and more disordered manner the more the disease advances. Thoughts follow in quick succession — so called flights of ideas.

In the melancholic depression the conditions are the opposite of those of the manic. Everything appears in a distorted, pessimistic light. There is lessened sexual desire. The feeling of self-satisfaction of the manic is replaced by feeling of regret and self-reproach, incapacity and diffidence. Thinking is painful and thoughts come slowly. In place of the overactivity and verbosity of the manic we find in the melancholic lessened activity and reticence to the point of so-called melancholic stupor.

Mild forms of manic-depressive psychosis are usually designated as hypomanias. Erotic manifestations are common. In girls this is manifest in the character of their address, correspondence and attitude to men. It occurs to the writer that many representatives of the "summer girl" of whom we hear so much and read about in the comic papers and magazines as becoming betrothed to another fellow each summer season, the engagement breaking up invariably at the end of the season, may belong to the manic-depressive type. That a manic-depressive enters a matrimonial engagement in a hypomaniacal state to break it again in a depressed state, there is no doubt about. The nonchalant attitude against reproof is another point worthy of note.

Among the physical changes the weight may show typical fluctuations. The weight usually goes down in a state of depression, differences between the maximum and minimum may amount to as much as 50 pounds. Appetite is usually increased in the manic and lessened in the depressed state. The skin is apt to be dry. The hair may be soft and pliable in the manic state and dry and brittle in the depressive. The eyes may show great brilliancy and even slight exophthalmos in maniacal elation as contrasted to the dullness in the depressed period. The depression of the lyric composer Franz Schubert, and of Goethe described in each case autographically are typical. Dr. S. E. Jelliffe refers to the cyclothymia characterized by dipsomanic periods of the writer Alfred de Musset.

Undoubtedly many cases of drug addictions are built upon a manic-depressive basis. Dr. Eva Charlotte Reid points out how the addiction of drugs observed in some prominent English authors was really to a great extent the result of periodic pathological states of the manic-depressive type. Thus in speaking of De Quincy's *Confessions of an Opium Eater*, she mentions the fact that these were written in a few weeks (while in the hypomanic state) but, "when the proofs were returned, his period of hypomania having passed, he spent six months in trying to correct one volume." She also states that Coleridge was interrupted in writing *Kubla Khan*, an opium dream, and never could complete the poem.

The Manic-Depressive Temperament or Constitution.

In the beginning of this paper, when giving the classification of the manic-depressive psychoses reference has already been made to the manic-depressive make-up, temperament, or constitution, which we almost invariably find in the patients subject to manic-depressive psychoses and which may also exist as a latent state, *i.e.*, without manic-depressive psychoses developing on its basis. A. Hoch deserves the credit of having called attention to this make-up. The latter quite particularly affects the emotional field; it is quite justifiable, therefore, to speak of a manic-depressive temperament.

The characteristics of this temperament are that those thus affected respond intensely to emotional factors both in feeling and in external expression thereof. They are easily moved to joy and grief, laughter and tears, in response to the emotional stimuli affecting them. They are also apt to have a high and hasty temper, getting easily indignant or angry, and as quickly regaining their placid mood. They have usually strong likes and dislikes. Their affections when engaged are usually very strong; they make intense lovers, very fond parents or children. Their mood is subject to rapid and abrupt changes under the influence of the impressions received.

Prophylaxis and Treatment of the Manic-Depressive Temperament and Psychoses.— In undertaking treatment of a manic-depressive it is essential to explain to him or her the nature of the mental make-up and some of its physical characteristics. Treatment should attempt to establish stabilization, mental and physical. An important point is the regulation of the process of nutrition and assimilation. To stimulate appetite and digestion, including intestinal peristalsis, Secretogen often does good. Syrup of Hypophosphites and thyroid extract may be used to stimulate a sluggish metabolism. A lubrication of the intestine and the contents by means of Russian oil is often helpful in addition to diet and other anti-constipation measures. An out-door life and exercise should be started in the very beginning. The mental therapy must be chiefly one of encouragement and of stimulating interest and good cheer.

The Co-operation Between the Spleen, Thyroid and Bone Marrow.— In a series of experiments upon rabbits, L. Asher and M. Dubois (*Biochemische Zeitschrift*, Nos. 3 and 4, 1918), found that in animals splenectomized, after the administration of large quantities of iron there was a transitory increase in both hemoglobin and number of erythrocytes. Added to the disappearance of the hemolytic factor the bone marrow is stimulated to a constant discharge of new red cells into the blood. Removal of the spleen results in no change in the number of white cells but in a decrease in the number of lymphocytes and an increase of the elements of the bone marrow. The differentiation of the leucocytes suggests an excitation of the leucopoietic system. A lymphocytosis takes place which the writers consider as a hypercompensation. Convalescence from anemia is shorter than in normal animals.

Removal of the thyroid results in a small decrease in the number of erythrocytes but the percentage of hemoglobin is not changed. A relative lymphocytosis results. The excitation from lack of oxygen does not change the blood formula even when the quantity of substance avid for oxygen is doubled. Convalescence in anemia is much longer in the absence of the thyroid.

When both spleen and thyroid are removed there is a slight decrease in the percentage of hemoglobin and a relatively greater decrease in the number of erythrocytes. If splenectomy is done some time before the thyroid is removed this does not occur.

The slight anemia in such animals is attended with an excitation of the bone marrow and in this condition it still produces new red blood cells. This excitation may be due to paralysis

Digitized by Google Original from HARVARD UNIVERSITY

of the thyroid system as a result of the thyroidectomy. White cells are diminished in number after operation. The maintenance of the balance of the types of leucocytes to each other results from removal of the spleen, the paralysis of the thyroid system only becoming effective after a long period of time. In removal of both, thyroid and spleen, an artificial dyspnoea occurs. A limited sub-oxygenation changes the hematologic formula unless the thyroids have been removed.

The convalescence from anæmia in such cases does not differ from that in a normal animal.

During the anæmia there is an increase in the white cells of the bone marrow in all cases except those in which the thyroidectomy has been performed. This is evidence of an over-acting bone marrow.

The results of the experiments suggest that there is an antagonism between the spleen and thyroid in the function of blood formation.

The thyroid accelerates; the spleen inhibits. The normal co-operation of the two results in a normal function of the hematogenous system. These experiments do not deny the possibility of other glands exerting an influence.

Vitamines, Unknown but Essential Accessory Factors of Diet.— Lecture delivered by Prof. F. G. Hopkins, of the University of Cambridge at Kings College on February 19, 1919.—*The Lancet*, March 1, 1919.

The science of the 19th Century has made it clear that it is the quality and not the quantity of food which is all important. The essential elements for human nutrition are proteins, fats, carbohydrates and mineral salts, but in addition there is needed something produced by plants in appreciable quantities. The nutritive importance of this substance is out of all proportion to the small amount in which it occurs in natural foodstuffs.

Beri-beri is very common in rice eating communities. That the cause was due to the removal of an essential food factor in the preparation of the rice was shown by Eijkman in 1897.

Feeding experiments on animals show that if the food consisted of pure protein, fats, carbohydrates, and mineral salts, the animals not only did not thrive, but, after a longer or shorter interval died, whilst an extremely small amount of this essential factor added to the diet converted it into a perfect nutriment. It is essential that these additions to the food be obtained from living tissue.

Many unsuccessful attempts have been made to isolate these substances though it is certain that they are actual substances and not qualities. They can be extracted, precipitated and redissolved but they cannot be completely separated from other substances. Their exact chemical nature and the exact amount needed for the body are not known. There are at least three of these substances, each one serving some particular function in nutrition. Two of these substances are soluble in water and one in fats.

The water soluble substance is removed when rice is polished and it is the absence of this which causes beri-beri. This is known as the anti-neuritic substance. Rickets in children, a disease of great national importance is associated with the fat soluble vitamine. Scurvy is another dietetic disease caused by absence of a water soluble vitamine.

The whole vitamine question is of the greatest importance in regard to the child population. Although we may not have beri-beri or pellagra and though scurvy might be rare, we have much ill health which stops short of definite symptoms, minor departures from the normal which occurred before the establishment of actual disease. The absolute absence of vitamines meant disease, their relative absence, malnutrition.

The Effect of the Maternal Ingestion of desiccated Placenta upon the rate of growth of breast fed Infants.

The results of a series of carefully conducted experiments by Frederick S. Hammett (*The Jour. of Bio. Chem.*, Dec. 1918) are interesting and conclusive. These experiments were undertaken in order to demonstrate whether placenta tissue administered to nursing mothers contains substances capable of affecting the growth of the infant. Previous experiments intended to show whether or not the maternal ingestion of placenta would affect the chemical composition of the milk led to the idea that the feeding of this substance to mothers had an effect upon the rate of growth of their breast fed infants entirely aside from the per cent. change in the determined constituents.

All patients received 10 grains of desiccated placenta in capsules t. i d. The results were tabulated only in the cases of mothers whose parturition was normal and whose infants were solely breast fed. The results were obtained by a comparison of groups of infants of approximately the same initial weight. The effect of the ingestion of the desiccated placenta by the mothers on the rate of growth of the breast fed infants was at once apparent. In each group not only was the post natal decline in weight less in amount, but also the gain in weight after the preliminary loss was greater in every case on every day than that recorded for the normal group, the mean increase over the normal per cent change in weight on the 13th day being over 60 per cent.

Comparative measurements of the mammae of mothers taking and not taking the desiccated placenta failed to show either hypertrophy of the gland or increased milk production in the case of women receiving the placenta substance. In view of this and since 30 grains per day of the dried material is negligible in so far as it furnishes material from which tissue can be built it is concluded that there must be contained in the desiccated placenta some substance or substances, capable of passing through the maternal organism with at least a part of its activity retained. Being secreted in the mammary gland it is passed on to the infant in the milk, there acting as a stimulus to growth. It is also concluded that the maternal ingestion of placenta causes an increase in the size of the infant.

The Relative Content of Antiscorbutic Principle in Limes and Lemons.— The results of experimental investigation and historical inquiry by H. Chick, E. M. Hume, R. F. Skelton and A. H. Smith (*Lancet*, November 30, 1918— 735) are conclusive in showing that fresh lime juice is far inferior to the juice of the lemon in the prevention of scurvy. Experiments on guinea pigs and monkeys show that lemon juice is at least four times as efficient. Preserved lime juice was found to have no value whatever.

The history of two Arctic expeditions, that of the Investigator in 1850 and that of the Alert and Discovery in 1875, shows that in the case of the former, supplied with lemon juice, there was almost complete immunity from scurvy during the first two years of great difficulty and privation. In the latter case, supplied with lime juice, scurvy was prevalent at the end of the first winter.

The curious fact is noted that the "lime juice" which enjoyed a deservedly high reputation as an anti-scrobutic in the British Navy 125 years ago was not lime juice at all but lemon juice. When the supply of this substance from Spain and later from the Mediterranean failed and the juice of the West Indian lime was employed it became evident that the genuine sour lime juice was inadequate as a prophylactic against scurvy.

BLOOD PRESSURE IN TUBERCULOSIS

W. O. Wilkes, M. D.

(*Texas Medical Journal*, March, 1919.)

It is well known that blood pressure is much below normal in tuberculous subjects, even in the very earliest stages. Possibly low blood pressure from other causes may bring about activity in old tuberculous foci. Fishberg says that when a low blood pressure is found "in an adult without any other assignable cause tuberculosis is to be suspected."

John Ritter "has found" (*Trans. Nat. Assn. Study and Prevention Tuber.* 1911, VII, 297), "hypotension in case of phthisis before physical signs, and even before elevation of temperature, were definitely demonstrable. This may be both cause and effect. All tuberculous subjects have low blood pressure, unless at the same time they have cardio-vascular disease. Statements as to the minimum pressure vary, perhaps because of a lack of uniformity in methods in taking the readings. The method of taking the reading must be described or the figures are without value, as many factors influence he reading in health and in disease. If some such method as that outlined by Brooks and Bleile" (*Jour. A. M. A.*, August 17, 1918) "could be universally adopted it would give a much greater value to blood pressure statistics."

Fishberg says "a registration less than 70 mm. of mercury is quite common" in incipient phthisis but I have not found it so. I have never seen a systolic blood pressure below 80 mm. in any adult individual, but I have found many tuberculous patients with a systolic pressure between 80 and 90. The ideal normal ratio between the pulse pressure, the diastolic and the systolic should be approximately 1-2-3. Fishberg may have observed a systolic pressure of less than 70 by feeling the pulse at the wrist instead of the method of auscultation.

Pottenger says "Blood pressure is lowered early in the disease although wide departures from the normal are rarely seen except in advanced cases." The statements of Fishberg and Pottenger are directly opposed. I believe the hypotension is caused by general physical weakness plus possibly some peculiar quality of the tubercular toxin; and that hypotension may be one cause for activity, and is always a sequel of tuberculosis. Pottenger's studies of blood pressure in 162 tuberculous patients and 20 non-tuberculous individuals gave for the non-tuberculous an average systolic pressure of 120 mm. and diastolic of 108. As these show only 12 mm. difference between the systolic and diastolic pressure it renders worthless the studies of the 162 tuberculous patients. The method of taking the reading should be described.

About 2 years ago I began taking blood pressure records of all tuberculous patients who came to my office by the ausculatory method using a Tycos instrument and a Bowles arm bracelet. The general systolic average of 319 patients examined in that period was 107.2 mm. and the diastolic 70.3 mm., giving a pulse pressure of 36.9. Both systolic and diastolic readings are below the normal for normal individuals.

The figures correspond closely to those of Burckhardt of Basel. I am partial to the method I have been using. If its 1-2-3 ratio is materially disturbed I search for the reason in the cardio-vascular-renal system if it cannot be accounted for by psychic or other influences of a transitory nature.

I do not believe that low blood pressure has any particular prognostic significance in tuberculosis. When a blood pressure is low at first and then gradually rises it is looked upon as a good indication, and when a blood pressure steadily falls under treatment it certainly gives a very grave prognosis. We do know that a very low systolic pressure without assignable cause points conclusively to tuberculosis, present or to come.

Digitized by Google Original from HARVARD UNIVERSITY

Book Reviews

Minor Maladies.—By Leonard Williams, M. D., Physician to the French Hospital, London, 4th Ed., Cloth, Pp. 402, $2.75, Wm. Wood & Co., New York; London, Ballière, Tindall & Cox, price 7/6 net.

That the latest edition of this very valuable work will meet with the favorable reception of the former editions is inevitable. It is a distinctly practical volume and may be read with profit by students and practitioners alike.

Chapters on Minor Glandular Insufficiencies and old age appear for the first time. The section on constipation has been rewritten. The book has a distinctly personal tone which makes one feel in intimate contact with its brilliant author. In facility of expression and in the beauty and force of its well balanced sentences the work stands as a model of fine English style. One is reminded of the manner in which Huxley gave to the world, in the same volumes, contributions to science and masterpieces in English.

The mission of the book is stated in the preface — "When I was first qualified, I went into general practice. I soon found that though moderately well equipped in the diagnosis and treatment of diseases which I seldom encountered, I was disconcertingly ignorant in those matters about which I was most frequently consulted. Pneumonia I knew, and Rheumatic Fever, and Typhoid; I was so well acquainted with Phthisis that I confidently recognized it in every trivial cough; and, so well versed was I in heart-murmurs that I was prepared to discover them and treat them — with a combination of digitalis and words of serious warning — even when they had no real significance. With knowledge concerning Tabes, Tumours and Trematodes I was full to overflowing; but I soon realized that I knew very little about a common cold, less about ordinary Indigestion, and nothing at all about rheumatic conditions. My knowledge of the subject of Personal Hygiene consisted in attributing to flannel all kinds of virtues, and to fresh air all manner of vices. In this dilemma I searched for a book which would lighten my darkness; but I found it not. I then determined that if time and circumstances should ever give me the opportunity of writing such a book, those of my juniors who found themselves in the same predicament should not want for such help as I might be able to afford them."

The chapters are devoted to

I. Colds, Coughs, and Sore Throats.
II. Indigestion.
III. Constipation, Diarrhœa, Vomiting and Giddiness.
IV. Rheumatism, Neuralgia, Headache.
V. Goutiness.
VI. Minor Glandular Insufficiencies.
VII. General Health.
VIII. Old Age.
IX. Some Drugs and Their Uses.
X. Insanity.

The chapter dealing with constipation and diarrhœa is especially valuable. The theoretical considerations have been given just enough space to emphasize the rational character of the treatment prescribed.

Minor Glandular Insufficiencies are considered in as brief space as is possible for this large and rapidly developing field. The author's estimate of the importance of this subject in medical practice is found in the preface.— "Still more earnestly do I believe that the study of the whole field of the Internal Secretions will enable us to detect and correct morbid tendencies with a degree of success which has been denied to the older methods. The microbe — the seed — has ruled the immediate past; the future is with the soil, the endocrine glands."

There must be few practitioners who will not profit by a careful reading of "Minor Maladies."

Diabetes and Its Dietetic Treatment. — By B. D. Basu, Major, I. M. S. (Retired), Ninth Edition (Revised and Enlarged), price Re 1 - 8, published by The Panini Office, Bhuvaneshvari Ashram, Bahadurganj, Allahabad.

Diabetes is very prevalent in India and Dr. Basu is evidently a pioneer in the new thought that is largely influencing the dietetic treatment of diabetic patients.

He strikes a keynote in his preface to the ninth edition when he says that it is a remarkable fact that the influence of vitamines on internal secretions in the etiology and treatment of that disorder does not seem to be recognized by the medical profession. If those who look upon diabetes as a disorder of nutrition are correct in their opinion, then the importance of vitamines in this malady will be easily understood. Internal secretions are concerned in the maintenance of nutrition of the system. Recent researches go to show that vitamines stimulate these secretions. Hence, the want of these substances unfavorably affects the internal secretions, and those articles of diet which are rich in vitamines will naturally do good in diabetes.

Dr. Basu is evidently in favor of the exclusion or, at least, a large limitation of meat in the treatment of this disorder and he also insists that the way the fresh vegetables are virtually manhandled in preparation for the table is a grave mistake. He is quite opposed to those physicians who recommend that vegetables should be boiled in several waters before they are used by the patient. He strictly disapproves of demineralization of food.

To Dr. Basu anything which relieves the alimentary toxemia, which toxemia is in his opinion due to errors in diet, is bound to be beneficial to the diabetic. Hence the importance of a vegetarian dietary and fruits in the treatment of the disease and the restriction if not the total withdrawal of meat, alcohol, tea, coffee, cocoa, etc. The book is instructive and stimulating.

The many friends of Sergeant Major S. C. Ritchie will be pleased to learn of his return to civil life and that he will resume his position as Manager of the London Office of G. W. Carnrick Co.

Raymond Fuller, now in Hong Kong, China.

Mr. Fuller is making a trip of inspection of the Distributing Agents of the G. W. Carnrick Co. in foreign lands.

Captain Joseph Eppler has just returned from active service and has resumed his position as Manager of our Shipping Department.

We regret to announce the death of Dr. Arthur T. Sherman at Phœnix, Arizona, December 12th, 1918, at 66 years of age.

Dr. Sherman was associated with G. W. Carnrick Co. as traveling representative for fifteen years. He had a large number of acquaintances and friends all over the United States among both physicians and druggists.

Dr. Sherman was a man of the highest personal character, beloved by all who knew him. He carried with him into his work an enthusiasm that made him a very efficient representative. He was a welcome visitor at the office of the physician and the store of the druggist for he had a "way with him" that appealed to everyone with whom he came in contact. Although a fluent talker, his earnestness was his chief asset and none could dispute his good faith in business.

My Service Flag

LUCY HAYS FURMAN, OXFORD, N. C.*

By the one blue star in my service flag
I have placed another today,
And now in the window where all may see
There are two —each of them precious to me
As I name them to God and pray.

The first star reflects the face of my boy
I see there faith, hope, love and truth,
And a heart all aflame with noble ideals
Dreams of brave service a good soldier feels—
And rose-colored visions of youth.

The other — oh, heart! a slip of a girl
She is young and tender and fair
There's a light in her eye not of sea, nor land —
Visions of faith in the touch of her hand,
And work she will do "over there!"

God, bless this lad and lassie of mine,
Whose smile from those blue stars I see;
May faith in themselves and faith in their God,
Sustain — e'en tho' they pass under the rod
And bring them back, safe home to me!

*Mrs. Furman is the wife of H. O. Furman, for several years a representative of our Company.

ON MEDI
OCT 27 19
LIBRARY

English Edition 190,000

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE INTERNAL SECRETIONS AND METABOLISM

Vol. IV **1919** **No. 2**

CONTENTS

Thyroid Therapy 25
The Role of Vitamines in Nutrition 27
Chemistry and the Endocrines 28
Endocrine Research 29
The Endocrine Glands and Bone Dystrophies 30
The Prevention of Scurvy 31
Indications for Operation in Diabetes 32
Duodenal Diabetes—An Exploded Fallacy 33
Medicine, a Determining Factor in War 34
An Improved Method for the Estimation of Sugar in the Urine and Blood 35
The Role of the Thymus in Pediatrics 35
Alkali Treatment in the Acidosis of Influenza 39
An Experimental Investigation on Rickets 40
Studies on Alimentary Hyperglycemia and Glycosuria 44
A Simple Urine Test for Acidosis 45
Theories Regarding Blood Pressure 46
Asthma as a Digestive Symptom-Complex 47
Phenol with Hydrogen Peroxid for Local Applications 48
Transplantation of Thyroid with Intact Blood Supply 48
Fat Redistribution in the Hypophyseal Type of Dystrophy Adiposogenitalis 48
Book Reviews 50

HORMOTONE

A successful treatment for disorders of menstruation and the climacteric.

Dose: One or two tablets three times daily before meals.

LITERATURE ON REQUEST

G. W. CARNRICK CO.

13-15 Laight Street, - New York, N. Y.

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

Vol. IV 1919 No. 2

THYROID THERAPY

The thyroid gland! The gland of romance, of genius, of vision, of action. What a potent influence it must have exercised upon the history of the human race. One cannot imagine the doing of "things worth while" with a hypofunctioning thyroid. It is the gland that dominates the entire endocrine picture. There is no combination to the strong box that contains the secret of good health that does not include the thyroid as one of the components of its mechanism. It is ubiquitous in its physiological activities. It is the general liaison agent that harmonizes and coordinates the offensive and defensive forces of the internal secretory system. Small wonder then that the thyroid plays first violin in the endocrine orchestra.

Since G. R. Murray first used it in the treatment of myxedema the scope of thyroid therapy has steadily increased. First it was employed only in those cases that showed definite objective evidence of thyroid insufficiency. In these cases the effect was markedly potent, — even if no curative results were obtained. These patients were in such a condition of congenital hypothyroidism that the product had to be fed to them for the rest of their lives in order that they might sustain something like a normal physiology. In other words, such medication was purely substitutive organotherapy. But as far as this medication and the results following it went, the effect of the treatment upon the welfare of the race amounted to virtually nothing. It is the minor case of hypothyroidism that under suitable thyroid treatment eventually pans out to the well being both of the individual and the species.

Hertoghe has said: "Thyroid insufficiency is essentially hereditary." He believes that when a factor such as hereditary syphilis, malaria, tuberculosis, alcoholism, exists in the parent as the initial activator, it exerts its influence primarily on the thyroid gland, and that it is the thyroid lesion which becomes the principal agent in the production of the miserable body. One can readily see, then, the far-reaching effects suitable thyroid treatment will have in these hypothyroid conditions, for it stands to reason that if the well-being of the parent is enhanced by proper doses of thyroid substance that the metabolic activity which is handed down from parent to child will be modified accordingly.

Leonard Williams emphasizes the important nature of minor thyroid insufficiencies. He says: "The broad lines of thyroid therapy are simple enough but the byways are fascinatingly complex." Levi and Rothschild are of the opinion that considerable importance attaches to minor thyroid insufficiencies for, unlike myxedema, they are very frequent. Here it is appropriate to refer to Hutchinson's teeth as an indication of insufficiency of the thyroid. Arnold Josefson has reported a case in which the development of well-marked Hutchinson's teeth could not be ascribed to hereditary syphilis but seemed to be wholly due to impaired function of the thyroid. Those who have examined a large number of school children will recall the comparative frequency with which Hutchinson's teeth are to be noted, and it is a debatable question whether or not this may be due to a far off syphilitic heredity and to consequent impaired thyroid function. Perhaps it would not be amiss to ascribe the condition, indirectly at least, to specific infection. Those who have noted the good effect of tiny doses of thyroid in children showing this symptom recognize that much can be done in shaping the child's physiological future by such doses. Oliver T. Osborne believes that among the conditions for which thyroid hyposecretion is responsible are some forms of eczema, some forms of asthma, infantile obesity, amenorrhea, senility and perhaps Raynaud's disease.

Thyroid therapy has justly attained fame in gynecological practice. As one of the most potent factors in genital development at puberty and as a regulator of menstrual function it can easily be seen that the control of thyroid function is of first-rate importance in establishing a normal condition in disorders of women. This holds true not only in the period of normal activity of the sexual glands but also can be applied very efficaciously at the climacteric.

Pitfield says that any woman approaching middle life, or in the fourth decade, who has had a history of backache, occipital headache, together with joint pains, dyspnea, asthenia, should be suspected of having hypothyroidism, especially so if she has amenorrhea or had had it during the menstrual life. Hertoghe has pointed out that it is a well recognized fact that thyroid insufficiency falls, in nine-tenths of the cases, on females. He says, "The thyroid has a great influence on menstruation, pregnancy, lactation and even uterine involution after childbirth. When the thyroid is normally active the menses are normal; when weak, menorrhagia sets in. The weaker the thyroid the greater the loss of blood. . . . A large quantity of thyroid stuff is wanted during the hemorrhagia period, and during that time cannot be given to the general keeping up of the body. We often see women who at ordinary times have a sufficient supply of thyroid secretion, run short during the menses, and show then, and then only, usual signs of thyroid defect." It is in such gynecological cases as these that thyroid medication shows at its best. Thyroid therapy will reduce to a considerable extent the anemic influence of the menstrual period and reduce considerably the loss of blood.

Thyroid medication has also proved an excellent remedy for sterility although here it has often been combined with ovarian substance to produce the best results.

The process of lactation also claims a great deal of thyroid secretion in the blood stream. Thyroid substance in distinctly hypothyroid cases will increase the quantity of milk, and has shown that other and far reaching results are also to be expected. Women who have good lactation will also have quick involution of the womb.

Robert Bell has reported cases of metrorrhagia which have cleared up beautifully under thyroid treatment and also reports the relief of dysmenorrheic conditions. He confirms what Hertoghe says as to the value of the thyroid in sterility and in poor lactation, and has also obtained some success with thyroid treatment in cases of uterine cancer.

In the treatment of nervous disorders thyroid therapy has also shown its value. Sehrt has reported nine cases of nervous disturbance in women in which marked benefit was received from thyroid treatment. In stuporous mental conditions thyroid substance in large doses seems to have a tremendous influence on metabolism. Eager, while finding it valuable in these conditions, found little benefit with it in the treatment of dementia praecox. Eager concludes that the most favorable cases for treatment are those of stupor or melancholia occurring in adolescence.

Constipation is another symptom that yields readily to thyroid treatment if the subject shows distinct evidence of hypothyroidism. This constipation is as a rule of the spastic type and may be cited in contradistinction to the diarrheas occurring in cases of hyperthyroidism.

Thyroid therapy in ophthalmic practice also has its place. Percy Dunn in the British Journal of Ophthalmology, January, 1919, points out that the eye in conjunction with the other parts of the body, cannot maintain its freedom from the influences of toxemia, whether it comes from intestinal putrefaction or septic foci such as pyorrhea alveolaris. One of the functions of the thyroid gland is to defeat autointoxication or autoinfection. The patient with sub-thyroid activity can and does easily fall a victim. In pyorrhea alveolaris a toxin is produced by the germs, a toxemia results and irido-cyclitis is liable to follow. He holds that keratitis punctata is most likely due to intestinal putrefaction. In these cases a family history of tuberculosis may be found in addition or as an underlying cause. Dunn finds thyroid treatment of great benefit in these cases. Corneal and pneumococcal ulcers also come under this category. Thyroid insufficiency is always in evidence at the menopause, and in these cases refractive defects corrected are not followed by ocular relief unless thyroid treatment be administered. Subconjunctival and subretinal hemorrhages are frequently, if not always, due to hypothyroidism. Recurrent retinal and vitreous hemorrhages seen in young males, accompanied by epistaxis and constipation are among the various signs of hypothyroidism. In Dunn's opinion thyroid prevents the advent of arteriosclerosis. In this connection T. Bodley Scott has said, "In women it is especially about the menopause that we shall find the minor symptoms of hypothyroidism; at the same time we shall find early symptoms of arteriosclerosis and of high blood pressure." The connection between hypothyroidism and arteriosclerosis is a very close one and the early treatment of the first will often prevent the development of the latter.

Perhaps no field of thyroid therapy is more promising than that in which it is employed in the treatment of physiologically defective children. These cases are of the "hypoplastic" type described by McCready in which "there is marked deficiency in height and weight, persistent subnormal or variable temperature, delayed puberty, high arched palate, scaphoid scapulae, delayed epiphyseal development as shown by x-rays, enlarged tonsils and adenoid growths, dulled or erratic mentality with the various stigmata of degeneracy." It can easily be imagined that a child of this description will be thoroughly handicapped under the stress of our modern civilization if proper measures are not employed to help him overcome the thyroid condition inherited from his parents. Various writers have cited cases of this description treated successfully with thyroid substance while others have combined thyroid with some of the other gland substances.

McCready says that his chief reliance is upon physical measures aided by organotherapy. He says, "A fund of knowledge is in process of acquisition which places endocrinology upon a rational foundation and furnishes concise indications for the administration of definite gland substances in definite disease conditions. While hypoplastic children very often present symptoms pointing toward dysfunction of individual glands, as the thyroid, pituitary, adrenals, etc., in the majority the implication is pluriglandular."

No matter what combination of gland substances is employed it may be taken for granted that thyroid substance always finds a place, and the good results following the exhibition of such a pluriglandular preparation as Hormotone is confirmation of the benefits to be attained with a rational measure of pluriglandular therapy.

Of the other conditions such as obesity of the endogenous type, skn diseases, premature senility, and many other conditions which are to a lesser or greater extent amenable to thyroid therapy, much could be written. Suffice it to say that a physician who is undertaking the treatment of a chronic disorder should carefully examine into the condition of his patient's thyroid function. In many of these cases such an investigation will yield good returns and once the diagnosis of thyroid insufficiency is made he will find thyroid therapy, alone or combined with that of other gland extracts, a veritable godsend.

As to the dosage of thyroid substance in hypothyroid conditions, there has been a great divergence of opinion but the consensus now seems to be that the doses of thyroid formerly given were much too large. Very few patients except certain types of myxedemics and lunatics will tolerate very large doses of thyroid. Indeed, Leonard Williams says it is a clinical fact, well recognized by those who have had any experience with the use of the drug, that the more the patient requires thyroid extract the smaller should be the initial dose. This author has been gradually driven back and back from the size of the dose he used to give and now seldom begins with more than ¼ of a grain three times a day. In the average case, and especially so with children, it is better to begin with a small dose, say ⅛ of a grain twice a day, and gradually increase the dosage until the symptoms of hyperthyroidism begin to manifest themselves. The dose should then be diminished and continued at a safe level, that is, just enough to maintain the improvement instituted in the patient's condition.

Dr. Mongiols sterilizes the hands with a paste made of equal parts of chloride of lime, carbonate of soda, boric acid, and talc. This procedure takes three minutes and can be used several times a day for four successive days without causing dermatitis. It permits of operating with bare hands, gloves being employed only in septic cases.

THE ROLE OF VITAMINES IN NUTRITION

The applications of chemistry and particularly of physical chemistry have played a leading part in the development of medicine in the last twenty years, and this has been most conspicuous in the field of general physiology and the physiology of nutrition. Stereochemistry, the new analytic processes for the proteins and amino acids and the application of the laws of mass action and osmosis to biology have all contributed to a better understanding of metabolism and give promise of still more valuable aid in the many remaining problems. Clinical observation in certain "dietary diseases" and biologic analysis by means of simple and purified diets, however, have shown that for the time being at least, a more rapid advance is possible by recourse to other methods. Failure of growth and causation of certain diseases have occurred with diets which chemical analysis showed contained the requisite food stuffs — protein, sugars, starches, fats, lipoids, and inorganic salts, and it became evident that there are certain indispensable elements of our food which as yet cannot be definitely ascertained by the usual methods of chemical analysis. These constituents are termed "vitamines."

Valuable experimental researches were made by F. G. Hopkins (1906), Stepp (1909), Fraser & Stanton (1907), and Eijkman (1897) which strongly suggested the presence of an essential, unidentified principle in diets just as necessary for growth and the maintenance of physiologic well being as the known food constituents. Hopkins, in a series of feeding experiments with a purified, simple diet, discovered that without the addition of milk, neither growth nor the maintenance of body weight could be obtained. Stepp found that mice fed with bread showed normal growth but that if the bread were extracted with alcohol death followed. The addition of the alcoholic extract again made the diet efficient. Eijkman produced experimental polyneuritis in pigeons with a diet restricted to polished rice, and later demonstrated that this condition could be cured by the administration of rice polishings. Fraser and Stanton had also administered alcoholic extracts of rice polishings in the treatment of polyneuritis. In 1911 Casimir Funk made elaborate researches in the causation of beri-beri, and as a result of his studies proposed the "vitamine theory." "Besides the ordinary food constituents, such as protein, fats, carbohydrates, lipoids and inorganic salts, to which our food is due, a number of substances can be found in small quantities which are as indispensable to life as the former constituents. These substances I have designated 'vitamines' and the diseases which arise from their lack as deficiency diseases or 'avitaminoses.'" Although direct evidence was available only in the case of beri-beri Funk assumed the existence of a specific vitamine in the case of scurvy, pellagra and rickets.

Digitized by Google Original from HARVARD UNIVERSITY

The existence of a number of specific vitamines is now one of the most debated questions in nutrition. McCollum has differentiated two essentially different classes of vitamines, one soluble in fats only and found chiefly in butter fat, egg yolks, fats of internal organs, and to lesser extent in the leaves of plants, and the other soluble in water, and found in many classes of plants, the germ of seeds, and in yeast. These have been designated "Fat Soluble A," and "Water Soluble B." Both are necessary in the diet for growth, reproduction and the prevention of disease. McCollum would include in the "avitaminoses" only beri-beri and a peculiar eye disease (Xerophthalmia). With his associates he has given convincing evidence that scurvy, pellagra and rickets are due, not to lack of a specific vitamine but to lack of other dietary essentials or to bacterial or other causes. In the case of scurvy, however, many observers postulate a specific antiscorbutic vitamine.

The source of the vitamine has been indicated, — milk, butter, egg yolk, seed germ, yeast, leaves of plants, etc. Articles of food containing these in relatively small amount are the tubers, endosperm of seeds, and fleshy muscles. The vitamines are synthesized only by plants and this points out the ultimate dependence of animal life upon plants. Milk and butter fats are rich in vitamines because the cow consumes large quantities of grass and leafy substances. The isolation of these substances in pure form and the determination of their formula has not been accomplished. They can be precipitated by phosphotungstic acid and be fractionated with mercuric chloride, silver nitrate and baryta. This precipitation seems to be specific for vitamines, which are nitrogen compounds, probably pyramidine bases analogous to uracil and thymine. (Funk.) Interesting experiments by Robert R. Williams with synthetic nitrogen cyclic compounds (hydroxypyridines) have shown that the administration of these substances exerts a marked curative effect in polyneuritis, approximating the curative effects of rice polishings. Williams points out the tautomeric changes exhibited by these substances and suggests that the anti neuritic properties point to isomerism as the reason for the instability of the "vitamines" in food stuffs. The quantity of such substances required is out of all proportion to the effect in relieving the symptoms of the disease. A few milligrams is sufficient to cure a pigeon with advanced polyneuritis. The work of McCollum suggests the necessity of a more careful scrutiny of facts and the elimination of many causes before postulating the lack of a specific "vitamine" as the etiologic factor in disease.

It is evident that we must view the problem of nutrition and proper diet from a new standpoint. It is no longer sufficient that our food intake be of proper proportion in fats, protein, water, carbohydrates, salts, and of adequate calorific value; it must also have the requisite "vitamine" content. The ordinary diet of Europe and America made up of seed products, tubers, roots, and meat, is as a rule sufficiently rich in the "Water Soluble" element but must be supplemented by "protective" foods to supply the "Fat Soluble" vitamine. Milk, butter, eggs, and fresh leafy vegetables are the sources of this essential element. Nutrition must fail and metabolism become abnormal if we ignore this teaching.

CHEMISTRY AND THE ENDOCRINES

The recent announcement in the press of the campaign for endowment for Harvard University emphasized the need for funds for the promotion of research in physiological chemistry. The stress placed upon this by one of America's most famous institutions of learning is indicative of the trend of modern scientific medicine. In perhaps no phase of medicine is the need for the advancement of our chemical knowledge greater than in that of the internal secretions. Falta says, "The deficient knowledge of the chemical nature of the active substances given off by the ductless glands constitutes the weak point in the knowledge of the internal secretions and explains why even today we are compelled to work with hazy ideas."

The isolation in crystalline form and proof of configuration of the active principles of the suprarenal medulla, adrenalin, ortho-dioxyphenyl-ethanol-methylamine is the first great landmark and was accomplished by the work of such able investigators as Fraenkel, Von Fürth, Abel, Aldrich and Takamine.

Thyroxin from the thyroid gland will always remain a tribute to the brilliant Kendall. The remaining ductless glands are the field of opportunity for the chemist. In the posterior pituitary lobe there is evidence that the active substance may be B-imino zolyl ethylamine. In the anterior lobe Robertson considers tethelin the active principle.

Less is known of the suprarenal cortex; a doubly refracting lipoid, cholesterol esters, fatty acids, cholin, etc., have been described but there is no proof of any active hormone secreted.

Of the active chemical principles of the thymus and gonads nothing is known. Until the precise chemical nature of the substances formed in these glands has been demonstrated, a clear understanding of their role in the endocrine system will not be possible.

A clear conception of the role of the endocrine system, the interrelation of the ductless glands, and the relation to the sympathetic and autonomic nervous system will probably be delayed until the fundamental work of the chemist has been completed.

The clinical evidence of the great importance of the endocrine system, the known facts of its place in the animal organism and the frequency and gravity of the diseases referable to it make it a field of live interest to the medical profession and to the public. The creation of special endowments in our medical institutions for research and teaching in the field of chemistry applied to endocrinology is one of the needs of medicine today.

RELATION OF THE ENDOCRINE GLANDS AND THE NERVOUS SYSTEM

As research in the physiology of the internal secretions has been so prolific of facts contributing to our knowledge of vital processes in general there has been the inevitable tendency on the part of the clinician to take the partly formulated theories and make therapeutic use of them. This eagerness to apply at once the knowledge thus far attained has apparently obscured, for the general practitioner, some of the most fundamental work in the whole field of the internal secretions — the demonstration of the close interrelationship between the ductless glands and the sympathetic and autonomic nervous system. That the dependence of the one upon the other is so close as to make necessary the conception that together they form a single vegetative system, is now apparent.

The sympathetic system consists of two chains of connected ganglia, one on each side of the vertebral column. They extend from the base of the skull down the cord and for the greater part of their course correspond to the origin of the spinal nerves.

The autonomic or para-sympathetic "consists of the cephalic portion which proceeds from the mid brain and the bulb — the oculomotor nerve, the pneumogastric and the chorda tympani — and of the sacral portion running from the chord — the pelvic nerve. This system of which the ruling element is the pneumogastric presents a functional antagonism to the sympathetic." (Internal Secretions and the Nervous System — Dr. M. Laignel-Lavastine.)

Hormones of certain ductless glands act on the sympathetic and others on the autonomic. Perhaps one of the best known illustrations is the action of adrenalin on the myoneural junction of muscles supplied by the sympathetic. Primary disturbance of either the nervous portion or the glandular portion of this system gives rise to functional disturbance and a variety of symptoms depending upon the parts mainly affected. The very closeness of the relationship of the parts make it probable that in any endocrine-nervous disturbance we are dealing not with a single gland or nerve region, but a pluriglandular and diffuse nervous affection. Psychic disturbance is perhaps a secondary phenomenon in this syndrome — differing in degree in proportion to the gravity of the endocrine-nervous disturbance. In cretins in Graves disease, etc., the mental condition may be one of the most evident symptoms.

To repair that 12,000,000 wastage in man power, the world will have to do the double quick and scatter a larger pottage of the June elixir of bridemating over the other months of the year. Heave a bit, ye chemists, and let's have a love pill, forthwith![†]

Well, what's the matter with Hormotone?

[†] *McK. and R. Drug Topics*, June, 1919.

Contemporary Comment.

ENDOCRINE RESEARCH*

This field is attracting a large number of individuals because of its newness and on account of its wonderful possibilities. These individuals are by no means all trained physiologists. Indeed, judging from the great variation in papers which are being published, an interest in the subject seems to be sufficient "training" for investigation in some instances. Perhaps no field is attracting a more diversely trained set of investigators at the present time. Physiologists, pathologists, zoologists, biochemists, physicians, psychologists and dentists are all taking their turn.

It is gratifying to know that the subject is of such general interest, but it is somewhat disconcerting to find that many who are untrained in physiology are attempting the solution of the physiological problems. Each may do very well in his own field, but he should be exceedingly careful about making interpretations in an unfamiliar field.

When one attempts to study a subject about which he knows little he is often led into fantastic speculation. As he learns more and more, cold facts serve him as ballast and tend to check speculation. It is true that judicious speculation may lead to new ideas and to new researches and thus to new discoveries. Yet so much speculation is useless or fallacious that unless tested by the ordeal of rigid experiment it should certainly not be published.

It seems that no field in physiology is filled with a greater amount of published speculation. This is undoubtedly due in part to our limited knowledge. But it is also due to a certain inaction on the part of some who prefer to take a chance on a lucky guess rather than to try out their assumptions. This is unfortunate, for it fogs the field. It is by tedious experiment that endocrinology or any science will be advanced, and not by brilliant guessing.

Study of the internal secretions is unusually difficult because these are mingled with the blood stream instead of being conducted through special ducts. Moreover it appears that only small amounts of the secretion are elaborated at any one moment. To isolate such a substance requires great patience and labor. And then to prove that one has the normal substance and not a modification presents even greater difficulty. But it will be necessary to isolate these secretions before we get at the fundamentals of endocrine physiology. Until that is done we shall be skimming on the surface of things. However, it seems that much can be learned before this stage is reached.

If one studies the endocrine literature he is struck by the contradictions among different

* *Endocrinology*, Jan., Mar., 1919.

investigators. If we stop to analyze the researches to account for this, we find that one or more of three causes may be present, viz., faulty technique, insufficient observations and incorrect interpretation of results.

It is fundamental in any science that the technique be unquestionable, but in a science so undeveloped as endocrinology it is especially requisite that this be true. Where a field is so new there are fewer facts available to correct mistaken methods. The result is that a faulty method may carry investigation far astray and wrong ideas gain prevalence. Therefore the methods in technique must be tested by carefully planned controls.

A second source of error, as mentioned earlier, lies in insufficient observation. By this we mean a paucity of experiments. Of course the requirements here vary with the nature of the problem. We must continually keep in mind that there may be not only considerable individual variation in the behavior of animals due to inherent differences, but that unforeseen modifications in the experimental conditions may give rise to disagreement. Multiplication of the observations as well as increase in the number of animals used will tend to eliminate this factor. Better a dozen experiments too many than one too few.

Perhaps the biggest factor for error is the personal one. However conscientious one may be this is bound to creep in, particularly in the interpretation of results. The greatest safeguard against this is to test the problem in every conceivable way. If you do not, someone else eventually will.

If these considerations were put into practice there would be far less confusion and contradiction and endocrinology would advance more rapidly. We believe that the time has come for the adoption of a more rigorous standard in endocrine research.

THE ENDOCRINE GLANDS AND BONE DYSTROPHIES.*

In the majority of bone dystrophies, if not in all, the skeleton is not the only structure which suffers. Unquestionably, its lesions are particularly striking, but other tissues, especially those which compose the locomotor apparatus, are likewise involved. The lymphoid and fibrous tissues, the ligaments, synovia, muscles, and tendons are more or less affected. Of the connective tissue, all the elements derived from the mesoderm show a solidarity and react under the same influences. Consequently, when bone changes, instead of being the result of a local accidental irritation, are due to general disturbances of metabolism, they rarely remain the only lesions. Their etiology often appears to be simple. For example, the process may be due to a nutritive perturbation, a badly chosen diet being often incriminated or a defective assimilation, infections, or chronic intoxications are frequently invoked.

It cannot be maintained that these causes alone are at work, and it is important in certain cases to take into consideration the changes or functional disturbances of the endocrine glands. The action of these glands on osteogenesis makes itself evident in many circumstances, and although it cannot be substituted for other morbid causes, the influence of which has long been known, it in no way lessens their importance or frequency, but often it enlightens us as to their mechanism and completes our knowledge of the subject. Whether the subject presents hereditary syphilis, an infection or chronic intoxication, nervous stigmata, circulatory disturbances resulting from improper feeding, one will invariably find indices of a general or local perturbation of the nutrition, and frequently this is due to changes or functional disturbances arising in some set of endocrine glands which are, *par excellence*, the regulators of metabolic changes. In the majority of cases the osseous dystrophies are due, not to a single given endocrine gland, but to several, so that they belong to a true pluriglandular syndrome.

The bone marrow possesses two functions, namely, it manufactures bone and blood. Indirectly by these processes it assures the solidity of the skeleton, its oyxgenation, and phagocytic defense. This hematopoietic gland, comprised in the alveoli, does not appear, it is true, to act on the nutrition by hormones. Its influence on growth, the development of the viscera, and the circulation, although less apparent than in the case of the thyroid, suprarenal, or hypophysis nevertheless exists. It is sensitive and reacts to excitations of a toxic or infectious nature, and from its double function causes changes in the skeleton. It is well known that in the anemias myelocytes and nucleated red blood corpuscles are found. But these reactions are all the more accentuated the more marked the lesions or functional disturbances of the endocrine glands. It is not as yet known whether the bone marrow inversely exercises a similar action, but this would seem rather unlikely, although it is certain that the latter suffers when the endocrine glands are involved. The influence of endocrine glands on ossification is unquestionable. In the first place should be mentioned the thyroid and hypophysis, but the testicle, ovary, suprarenals, thymus, and pancreas have equally an undoubted, although, perhaps, a more limited action. On the other hand, the combined action of several of these glands may cause various disturbances too numerous to be mentioned.

IODIN AND THE THYROIDS*

Iodin and its compounds have been employed for nearly a century in the treatment of disorders associated with the thyroid glands. When Baumann of Freiburg, in 1895, discovered that the thyroid glands contain iodin, there was immediate speculation as to the relation of this chemical element, not found elsewhere in the body in equally appreciable amounts, to the glandular function. The earliest assumption was that the "active principle" of the thyroids contains iodin. Some thyroids contain almost none of the element; but it has been noted that such glands used therapeutically do not seem to manifest the same physiologic activity that is exhibited by thyroid preparations containing iodin. In other words, the potency to produce certain physiologic effects after administration of thyroid has seemed to several investigators to depend on or parallel the iodin content. The active product isolated from the thyroid by Kendall of the Mayo Clinic is rich in iodin. Gudernatsch has recorded the remarkable observation that the feeding of thyroid extract to tadpoles brings about rapid and marked metamorphoses in these animals. Swingle has followed this with the further demonstration that iodin and its compounds fed to the larvæ of the frog and the toad stimulate metamorphosis in these animals very rapidly; that is, the results resemble those induced by the hyperthyroidism already described. It has been assumed that all such effects are brought about by the intermediation of the thyroid glands in the animals fed. Allen has shown that thyroidectomized larvæ fail to undergo metamorphosis, but instead permanently retain their larval characters. But Swingle has since found that when inorganic iodin is fed to thyroidless larvæ of toads, a metamorphosis occurs in an abnormally short time, despite the complete absence of the thyroid gland in them. He therefore concludes that if animals without the vestige of a thyroid gland are stimulated to complete metamorphosis in an abnormally short time by iodin, it would appear that iodin functions within the organism as a hormone itself, and that the gland functions chiefly for storage purposes. The evidence from the thyroidectomized larvæ indicates, Swingle adds, that the animal body is capable of utilizing iodin directly without the intermediation of the gland. It is admittedly little more than speculation to transfer the observations on the development of these lowly forms to the thyroid function in man. They are not entirely incompatible with the view that, so far as iodin is concerned the chief function of the thyroid is one of storage. However, it seems more than likely at present that the unique organic combinations of the element obtainable from the gland are far more potent in their effect on metabolism than are the simple salts of iodin. Whether, therefore, iodin functions best through the intermediation of the glands whereby its potency is augmented remains to be considered.

---

* *N. Y. Med. Jour.*, May 24, 1919.

* *Jour. A. M. A.*, June 28, 1919.

THE PREVENTION OF SCURVY*

During the past few years scurvy has been more or less common among the armies in the near and far East. In consequence, the etiology and treatment of the condition have been studied quite closely. Of course, it has been known for some time to be a deficiency disease, that is a disease due to a deficiency or lack of vitamine content in the diet, but this fact has been strongly emphasized by the investigations made in Mesopotamia and elsewhere. Also dietetic treatment has further clinched the point that scurvy is a deficiency disease. The Food Committee of the British Royal Society issued a short time ago the following conclusions as to scurvy, based on investigations made at the Lister Institute, London: (1) Scurvy, like beriberi, is a "deficiency disease" and is due to the continued consumption of food lacking in an accessory food substance or vitamine. (2) This vitamine is contained in a number of fresh foods, in largest amounts in oranges, lemons, and fresh green vegetables, in considerable amounts in roots and tubers, such as turnips, potatoes, etc. It is deficient in all dried and preserved foods. (3) It is destroyed by prolonged heating. Thus potatoes in stews would be devoid of vitamine, but if boiled rapidly will still contain a small quantity. Alkalies rapidly destroy antiscorbutic properties. Soda should not, therefore, be added to water in which vegetables are soaked or boiled. (4) Before the onset of definite symptoms of scurvy there is a period of debility and weakened resistance to disease. Cases of debility in any body of troops without sufficient cause should at once direct attention to the diet. (5) West Indian lime juice as ordinarily prepared is useless. Fresh limes have an antiscorbutic quality but their efficiency is only one-fourth that of lemons. Orange juice is as effective as lemon juice. (6) Potatoes and root vegetables have a distinct value in the prevention of scurvy, much less, however, than green vegetables or fresh fruit juices. (7) Pulses — beans, peas, and lentils — in the dried condition have no antiscorbutic properties. If, however, the dried seeds are soaked in water and allowed to germinate for a short period, they develop the antiscorbutic vitamine. At the same time these pulses are also rich in the vitamine which prevents beriberi, and are moreover, valuable foods. (8) The antiscorbutic value of fresh meat is very low in comparison with fresh vegetables and fruit. Tinned and preserved meats possess no antiscorbutic value. Frozen meat, while more valuable than preserved meat, must be considered inferior to freshly killed meat. (9) The destruction of antiscorbutic properties of foods during the process of cooking depends upon the time of cooking and temperature employed. All foods, especially vegetables, should be cooked in as short a time as possible at boiling point. Slow methods of cooking, such as stewing or simmering below boiling point, should be avoided. Potatoes should be plunged into boiling water and boiling continued for twenty or thirty minutes after boiling point had again been reached. Frozen meat should be roasted when practicable.

These findings go to show that views as to the value of the various foods from the nutritive standpoint have changed greatly within the past ten or twenty years. The vitamine content of food must not be greatly impaired or nutrition will not only be unsatisfactory, but beyond a certain point pathological conditions will be produced. Meat has been shown to be in many respects, and especially so far as vitamines are concerned, inferior to other foods which not long ago used to be regarded with thinly veiled contempt. The pulses, either fresh or germinating, have been elevated to a high position among the food products and are as economical as they are nutritious. The report from which quotations have been made gives some useful advice as to cooking, an art concerning which there is a great deal of ignorance, and particularly with regard to cooking in such a manner as to preserve as much as possible the nutritive properties of the food. Lastly, it was shown that canned and dried foods do not contain the amount of nourishment which is contained in fresh foods, and that so far as vitamine content is concerned they are useless. Our ideas as to food must evidently undergo a great deal of revision from all points of view.

---

* *Medical Record*, June 28, 1919.

INDICATIONS FOR OPERATION IN DIABETES*

The indications for surgical intervention in diabetes mellitus are discussed by Blum, who remarks that this question may be one of the most difficult problems which the practitioner has to confront. Apart from urgent cases in which an operation is imperative, such as strangulated hernia or perforative appendicitis, hesitation may arise as to whether an operation is justifiable or as to the period at which it should be performed. The difficulties are all the greater as diabetes and the surgical affection have a reciprocal influence upon one another and a vicious circle is created.

Should the operation be carried out at once to remove the lesion and at the same time the causes which have an unfavorable action on the diabetes? Or, on the other hand, should an attempt be made to render the urine free from sugar, or at least to reduce the glycosuria so as to cause an improvement in the lesion and thus render the conditions more favorable for operation? Much may be said in defense of either step. Numerous instances have occurred of surgical affections in diabetes which have healed spontaneously after disappearance of sugar from the urine, while, on the other hand, it often happens that after successful operation the diabetes takes a mild course and shows an improvement characterized by diminution of glycosuria and disappearance of the acetonuria. The difficulty of deciding in these cases is increased by the fact that a surgical operation exposes the diabetes patient to great danger, which is chiefly connected with the anæsthetic and operative shock. Moreover, the preparation of the patient constitutes a psychical trauma which may act very unfavorably on the disease.

As regards the anæsthetic, ether is to be preferred to chloroform, though cases of diabetic coma following the use of ether are by no means rare. Spinal and local anæsthesia present certain advantages, but these are counterbalanced by the great likelihood of shock ensuing. Blum is of opinion that in mild cases of diabetes characterized by a slight degree of glycosuria and the absence of acetone bodies abstention is indicated, and an attempt should be made to cure the glycosuria. On the other hand, in severe cases characterized by a high amount of glycosuria and the presence of acidosis operation should be performed as quickly as possible. The same applies to diabetes complicated by nephritis.

MEDICAL ASPECTS OF THE FOOD PROBLEM*

Because peace is now assured it by no means necessarily follows that the millennium is in sight. So far as the question of food is concerned, the world is in no better condition now than when war was in active progress, indeed, in some respects, at least, it appears to be in a worse position. In Germany, Austria, Rumania, Poland, and even in Belgium, a condition of semistarvation exists. Moreover, Russia, which has been one of the great granaries of the world, owing to her internal turmoil, is unable to feed adequately her own population. In fact, the whole of Europe is looking to North America and South America and Australia to feed her population. It must be also borne in mind that means of transportation by sea are woefully inadequate for the occasion. Therefore, we must possess our souls in patience and anticipate a considerable period of lean days yet. The problem of the food supply itself has not been solved, nor, it may be said, has the solution been found of the medical aspects of the food problem.

It has been asserted with some vehemence that the scarcity of food in Europe has had a good effect upon the general health. Up to a certain point this statement is true, or partially true. Many persons, in the piping days of peace, were in the habit of eating too much, and especially of meat and of taking too little exercise. These individuals were benefited, to some extent, by this compulsory abstinence. But, on the other hand, lack of food or the ingestion of comparatively non-nutritious food, obviously can do no one good.

The war has afforded splendid opportunities for gauging what constitutes the minimum amount of food on which a man or woman may live and do hard work. The physiological requirements of the human animal, under varying conditions, have been ascertained with some degree of accuracy, although it may be stated definitely that the last word on the subject has not been said. It has been learned, however, that some long cherished ideas as to the value of this or that article of diet, must undergo a good deal of revision. For example, the fetish of highly milled white flour has received a setback from which it will probably never recover. Other food stuffs which in the old prosperous days were looked at askance, mainly because they were cheap, have been shown to be very nutritious.

---

* *The Lancet*, May 31, 1919.

* *N. Y. Med. Jour.*, May 24, 1919.

In a discussion on war food which took place under the auspices of the West London Medico-chirurgical Society, on April 5, 1918, reported in the *West London Medical Journal*, October, 1918. Dr. Leonard Williams made some remarks which will doubtless meet with the approbation of some of our readers. He deprecated a hard and fast acceptance of all the tenets comprised in the present day theory of scientific feeding. He pointed out that the principle of proteins, carbohydrates, and fats did not explain everything. He further confessed to having no belief whatever in the theory of calories, which he said was clearly based on the assumption that the human gastrointestinal tract was a test tube. He was of the opinion that in our present estimate of dietetics there was a tertian quid, and he went on to say that he had no doubt that the tertian quid was supplied by the consideration of the vitamines, substances which had been described chiefly by American writers. He expressed his belief that the application of the principle of present dietetics was this, that if people would eat food which contained vitamines in large quantities they were able not only to sustain, but to enjoy life on an amount of proteins, carbohydrates, and fats, which, in the absence of vitamines, would be ludicrously inadequate.

Williams, no doubt, is somewhat too iconoclastic as regards scientific feeding, but it is manifestly true that too great regard may be paid to rationing an individual from the point of view of his physiological requirements alone. Appetite inciting food is essential to some, such as meat essences, beef tea, and so on. Custom also plays an important role in feeding. Conditions of life must be always considered and the question of climate must not be overlooked. Also the personal equation is not altogether a matter of indifference. Reviewing the food problem from the medical standpoint broadly, it may be said that the exigencies of war have brought into prominence two outstanding features, that animal food does not occupy the high place in the estimation of scientific investigators, and of practical men that it formerly held, and that the vitamines play a predominant, although as yet not thoroughly understood, part, in the maintenance of nutrition.

High Blood Pressure: Organotherapy is a potent weapon in the treatment. Here one is copying nature's methods. Physicians who use Secretogen and Hormotone Without Post-Pituitary in the treatment of high blood pressure get results that astonish themselves and delight their patients.

DUODENAL DIABETES — AN EXPLODED FALLACY*

The introduction of the expression "duodenal diabetes" into the literature of medicine is due to the late German physiologist Eduard Pflüger of Bonn. Having observed that section of the intramesenteric nervous connections between the pancreas and duodenum in the frog may, under certain circumstances, give rise to a glycosuria, he called into question the existence of a pancreatic diabetes. Minkowski subsequently silenced this charge against what had been regarded as an established demonstration, by a successful experimental extirpation of the duodenum without producing a state of diabetes so long as a portion of pancreatic tissue was left intact in the body. Duodenectomy is, however, a dangerous procedure; and, since scarcely any cases of prolonged survival of the subjects are on record, the possibility that the duodenum is indispensable for physiologic well-being has remained to be definitely considered. Thanks to the ingenious operative procedure described by Moorhead and Landes in a recent issue of *The Journal*, complete removal of the duodenum in consecutive operations is permitted. The jejunum is made to serve as a substitute for the duodenum and to receive the pancreatic and biliary secretions through transplanted ducts. The experiments made by the authors at the University of Chicago show that "dogs thus operated on will live in a normal state of health. The duodenum, therefore, is not essential to life." The outcome reminds us of the comment of von Fürth of Vienna on the subject of duodenal diabetes: "Strictly speaking, nothing at all has been gained in this whole campaign fought with an array of heavy artillery of authority and between strategists of note, except the re-establishment of a fact that has long been known — the influence of nervous irritations of all sorts causes the liver to discharge its supply of carbohydrate which sometimes gives rise to glycosuria."

THE ORIGINAL UNCLE SAM

Few people know that Uncle Sam was a real personage and that his name was Wilson.

On the office of Miss Willard's Seminary in Troy, New York, the editor has seen a bronze tablet which states that, "On this spot was the home of Samuel Wilson, the original Uncle Sam. He was a dealer in cattle and had a contract to supply the Federal Army with beef in the war of 1861-1865. The shipments bore the mark "Samuel Wilson" and the boys adopted Uncle Sam as their patron saint."

* *Jour. A. M. A.*, June 7, 1919.

"In therapeutics we often adopt measures merely because we know by experience that they succeed. An explanation of the *modus operandi* comes later, and the correct explanation often much later still." Leonard Williams, M. D.

Articles of Interest

MEDICINE, A DETERMINING FACTOR IN WAR*

By Alexander Lambert, M. D.

In his presidential address before the American Medical Association, Dr. Lambert reviews the problem before the medical profession today. He points out the splendid work of the profession in the war and the work of the Surgeon General's office, the Council of National Defense and the A. M. A. in accomplishing the mobilization of 35,000 medical officers in the army and 3,000 in the Navy.

Work of Local Boards

The great work of the local boards calls for commendation. Of the 2,124,293 who were sent to camps by the local boards and were then subjected to the careful examinations of experts, 91.9% were accepted and only 8.1% rejected.

Success of Preventive Medicine

Few realize how crucial has been the test of preventive medicine in the war just finished. The death rate from disease has been held down as never before. The statistics available show conclusively that the great scourges and plagues of former armies have been held in check, i. e., typhus fever, cholera, recurrent fever, typhoid, scurvy, malaria and small pox. Influenza with pneumonia has been the one uncontrolled epidemic. To appreciate fully the meaning of this result of preventive medicine and what the American medical profession has accomplished, let us study the battle casualties and disease rates of former wars, and, by this contrast, appreciate the achievement.

In former wars from the middle ages to the present the plagues and epidemics were more deadly than the armed opposition. Emperor Frederick Barbarossa saw an army in Italy annihilated by sunstroke. Ten years later pestilence swept another army away. In the 30 years war bubonic plague decimated the Swedish forces and compelled their withdrawal. In modern times disease so disorganized the French army at Sebastopol that it was a large element in concluding peace before the aims of the campaign were accomplished.

The death rate in our Civil War of killed and dying of wounds is given as thirty-three to the thousand, the disease death rate as sixty-five. In the Spanish War the death rate from battle is five and the death rate from disease 30.4 to the thousand. In the present war, taking the statistics up to March 28, 1919, we find the rate of death from wounds received in action is 14.191 and that of death from disease is 14.797 to the thousand. This includes the army on both sides of the ocean. The statistics of the American Expeditionary Forces, with an average strength of 975,716, reveal a rate of death from wounds in action of 31.256 to the thousand and a death rate from disease of 11.233. Of those who died of disease, pneumonia claimed 9.146 to the thousand.

Modern Control of Destructive Diseases

Medical science has today, therefore within its grasp the power to control the diseases which, in former times, decimated warring armies and spread out from these armies among the noncombatant populations. Formerly, when war broke out, it was almost inevitably followed by some dread pestilence among the civil populations of the countries in which the war was waged. By proper sanitation and preventive inoculation, dysentery and cholera can be abolished; by vaccination armies can be protected against smallpox. Body lice disseminate typhus, recurrent fever, and trench fever, and by proper disinfection of these vermin these diseases cease to occur. Through sanitation and preventive inoculation, typhoid fever, the scourge of the two previous wars, is absolutely controlled, and this includes also paratyphoid, which has been recognized as a separate entity only since the Spanish-American War.

Lessons Learned in Determining Action in Future

The salvage of human beings and the protection of troops from disease is the great problem.

Educational Needs of the Medical Profession

One lesson of the war which stands out with great distinctness is the necessity for the American Medical Association to continue its unceasing struggle to raise the standards of medical education in this country. Such are the increasing demands made on the medical profession that the young men entering it today must realize that the broadest and most excellent education obtainable is none too good. It is not asking too much to require that all medical schools which are permitted to continue should soon be raised to the A class.

Need of Improved Organization

One very important duty to be performed soon is the re-organization of the Medical Reserve Corps and the rearrangement of the medical reserve officers and of the medical officers of the National Guard into one National Reserve Corps.

Relation of Red Cross to Army

The relationship of the Red Cross and the army is not generally understood. The Red Cross is not a private society supported by private contributions, but is a governmental body incorporated by Congress, with a definite function, that of giving voluntary aid to the soldiers and sailors of the army and navy during war. It differs from other governmental functions in that it is not supported by Congressional appropriations, but by voluntary contributions. Many of its functions and their limitations are defined in international treaties with other nations.

---

* *New York Medical Jour.*, June 14, 1919.

The war has shown that the Red Cross has proved an excellent stopgap for supplies and a source of all kinds of emergency and surgical supplies and relief.

National Control of Preventable Disease

I desire to draw but one more logical deduction from the medical lessons of this great war, and that in reality is the climax toward which all points. That is, if this nation, through its present medical knowledge, has within its grasp the power to control communicable, and hence preventable diseases, there must be established a nation wide controlling organization for this purpose, a National Department of Health.

It is the duty of the American Medical Association, and of each member of each State association, to urge on Congress the establishment of a National Department of Health.

AN IMPROVED METHOD FOR THE ESTIMATION OF SUGAR IN THE URINE AND BLOOD*

By P. J. Cammidge, M. D.

Further experience with the volumetric method for estimating sugar I described in *The Lancet* of April 21st, 1917, p. 613, has confirmed the accuracy of the results given with quantities above 0.5 per cent., but with percentages below that amount too low a reading may be obtained unless further precautions than those described are taken against oxidation, especially in warm weather. The original experiments in working out the method for blood sugar happened to be made with freshly distilled water and in the winter; later it was found that when distilled water which had stood exposed to the air for some time was used with test solutions of sugar containing under 0.5 per cent. the readings were lower than they should have been, and that the variation from the expected result differed with the age of the water and the temperature of the air. Eventually it was proved that the error arose from dissolved oxygen in the water and solutions employed in the test.

When, therefore, a urine is expected to contain a low percentage of sugar, under 0.5 per cent., and with all blood and other fluids containing smaller amounts, the water to which the iodine solution is to be added should be thoroughly boiled, to expell dissolved air, and cooled, immediately before the estimation is to be made. It is also advisable that the alkaline copper solution for sugar estimations with urine should be boiled in a small conical flask, provided with a loose funnel as a stopper, instead of in a beaker as previously described, and that the required amount of urine should be run into the boiling fluid from a pipette when the air dissolved in the solution, and contained in the flask, has been expelled.

With blood, etc., the 7.5 c. cm. of filtrate and 1 c. cm. of sodium carbonate solution are boiled together in a similar way in a small conical flask fitted with a funnel-stopper, and the 1 c. cm. of modified Benedict solution is added after they have boiled for a few seconds. The water used for diluting the iodine solution and for washing out the flask, etc., should have been recently boiled and cooled. With these additional precautions the method gives uniformly reliable figures, even with the small amount of sugar in normal urine and blood.

THE ROLE OF THE THYMUS IN PEDIATRICS*

By Murray B. Gordon, M. D.

. . . The thymus is susceptible to all infections and conditions affecting the general nutrition of the body. Pathological involution often results. In acute diseases like starvation, pneumonia, acute nephritis and acute infectious diseases, this change is usually followed by a return of the organ to the normal. In chronic disorders, however, a return to the normal does not take place, the gland instead undergoing a permanent sclerosis with resulting permanent involution. Hereditary syphilis, tuberculosis and diphtheria produce atrophy and degeneration. Respiratory diseases (according to Charkowski) if not tubercular, do not interfere with the development of the thymus. In the course of an acute disease the thymus may be decreased to one-fifth or one-sixth of its normal weight.

Function. The function of the thymus is still an open question. There is a tendency among investigators lately to question the former findings of Klose, Vogt, and Matti that it is an organ of internal secretion and to give it now the same or similar function as that possessed by other hematopoietic organs like the spleen and lymph glands.

Sajous thinks that it is not the source of an internal secretion. He considers that the "function of the thymus is to supply, through the agency of the lymphocytes, the excess of nucleins which the body, particularly the osseous, nervous and genital systems, requires during infancy, childhood or even later, if need be, to construct the nuclei of its cells." He thinks that the thymus due to its richness in nucleins, takes part in the oxidation and auto-protective processes of the body, and that it has some important relation with metabolism as regards the role of phosphorus in the body. Conclusive evidence on these points, however, is lacking.

The experiments of Klose and Vogt seemed to indicate that the thymus is essential to life, has a profound influence on growth and development of the body and presides especially over calcium metabolism of bone. They found that the removal of the thymus in animals was followed by marked disturbances in growth, that the animals developed a condition resembling rickets and showed well-marked changes in the adrenals and thyroid. The thymus was removed in ten days' old puppies. This was followed by a latent period of two to three weeks, then by a condition of adiposity lasting about two to three months, this in turn giving way to a cachexia and an impaired mentality resembling idiocy and finally culminating in death in about four months. It was claimed that extirpation of the thymus in children is followed by the same results. Klose and Vogt considered that the bone and other changes were due to an acid intoxication and that one of the functions of the thymus is either to inhibit the formation of nucleic acid or else to neutralize its excessive formation. They also claimed that the total removal of the thymus in the young resulted in rickets, but that in adults extirpation was followed by osteoporosis and osteomalacia. Basch, Matti, Gudernatsch, Rochford and others have reported substantiating observations.

---

* *The Lancet*, May 31, 1919.

* *Endocrinology*, Oct.-Dec., 1918.

Considerable experimental study in the laboratories of other careful investigators has failed to confirm these results. Park assails the work of Matti, Klose and their followers on the ground that the changes found in the animals were due to poor hygienic surroundings in the kennels. Some of the results were obtained by extirpation of the thymus in guinea pigs. Park made a careful study of serial sections through the neck region of this animal and showed that a guinea pig has so much accessory thymus tissue as to render complete thymectomy impossible. Earlier reports of results following thymectomy in this animal must therefore be interpreted as partial only.

Pappenheimer claims that removal of the thymus does not produce disturbances in growth or development and that no pathological changes are found after thymectomy anywhere in the body. He arrived at the following conclusions:

"1. In some species of animals, complete removal of the thymus arrests growth, especially the proper development of the skeletal system.

2. We have no data as to results of removal in human beings.

3. We have no experimental work which gives us a clue as to the effects of an excessive or perverted secretion.

4. We are not yet justified in assigning to the thymus a definite role in the causation of any known disease."

E. R. Hoskins, using albino rats, found that thymus feeding resulted in no constant effects on body weight or on that of individual organs.

Park extirpated the thymus in animals and found that no difference could be detected between the experimental animals and the controls, either as to procreative activities, growth or conditions in endocrine glands. He did not obtain rickets in any of his thymectomized animals.

Swingle fed fresh thymus and powdered commercial thymus to 150 frog larvæ and found that it had no effect on growth or on the gonads.

Inter-relationship between Thymus and Organs of Internal Secretion

Investigators are divided as to the relationship between the thymus and the organs of internal secretion, depending upon their belief as to whether or not the thymus itself has an internal secretion. Basch, Matti, Gudernatsch, Paton, Henderson, Rachford and others claim that they have demonstrated this relationship and believe that the thymus has an inhibitory action on the thyroid, adrenals, gonads, spleen and pancreas. Halnan and Marshall, however, observed no pathological changes following thymectomy; their experimental animals did not show any abnormalities of growth or development after the removal of the thymus, nor did removal of both testes and thymus in young guinea pigs alter the growth of the animals up to the time of sexual maturity. Park, Swingle and others also found that the thymus persists after castration.

Heidinger found seven cases of enlarged thyroid in twelve cases of thymic death in the new born. Garre and Capelle found 95 per cent. of fatal cases of exophthalmic goitre to have enlarged thymuses. There have been many other reports of a combination of exophthalmic goitre and thymus hyperplasia. (Virchow, Crotti, Hart, Weber, Gluch and others.) Mackenzie noted that in 36 post morten examinations of cases of exophthalmic goitre, the most constant feature next to thyroid enlargement was the presence of an enlarged or persistent thymus. Hart believes that there is a pure thymogenic form of exophthalmic goitre.

Behlow makes the statement that he has looked for thymic enlargement in all cases of glandular dyscrasia and that he has found it in several instances. He also thinks that X-Ray examination of the chest in cases of Addison's disease will show an enlarged thymus.

Myasthenia gravis, while not properly a disease met with in children, will be considered here, as it may be the result of a condition which has its inception during childhood or even in utero. Bell quotes Starr, who had reviewed 250 cases of this condition and had noted a pathological state of the thymus in 28 of the cases that came to autopsy. Of 56 autopsies published since then, the thymus was found to be enlarged in 17 and contained a tumor in 10. Hart thinks that in this disease the affected individual has a "lymphatic constitution;" in other words, is constitutionally inferior and therefore predisposed from birth to the development of such a condition. He also believes that the thymus in myasthenia gravis exerts a pathological function and is frequently, if not always, the cause of the disease. He states that the removal of the thymus produces a cure, but admits that there are cases without thymus hyperplasia. His theory has not been substantiated

Absence or deficient activity of the thymus, according to several observers, produces mental disorders in children. Bourneville found that in

28 mentally defective children, the thymus was absent. He has shown, based upon the findings of a large number of autopsies, that in over 70 per cent. of mentally defective and epileptic children, the thymus was absent. Katz found that there was a normal thymus in every case of 61 normally mental children from 1 month to 13 years old, as shown by autopsy. Sajous believes that, while no type of idiocy can be referred to deficiency of any one gland, still, "deficient activity of the thymus results in deficiency of nucleins supplied to the brain through lymphocytes, causing idiocy." Harrower makes the statement that thymus hyperplasia is accompanied by defectiveness and by the hypoplastic type of individual.

Status Thymo-Lymphaticus

Post mortem examinations of cases of sudden death have in several instances revealed an enlarged thymus as the only pathological finding, with or without an accompanying hyperplasia of the lymphoid tissue of the body. This has led many to accept the thymus as the causative factor of the death, explaining it on the basis of physical compression of the trachea or of the great vessels in keeping with the anatomical arrangement of the thymus.

Antero-posterior diameter of the superior opening of the thorax is 2 to 3 centimeters. A finger placed behind the episternal notch can feel the impact of the rising thymus. The thymus follows the up and down movements of the trachea and larynx during acts of coughing, swallowing and hyper-extension of the head. Grawitz believed that it was possible for the thymus to become wedged in between the upper part of the sternum and the vertebral column in such a way as to compress the trachea at that point, causing death from asphyxiation; this space is now known as the "critical space of Grawitz." Another place taken as a critical space where the trachea may be compressed is at the crossing of the innominate (Klose, Matti). Death may also be caused by direct pressure on the base of the heart. Herrick suggests that the respiratory symptoms are probably caused by pressure on other organs, for how can one explain the fact that the trachea, which is cartilaginous, should suffer compression and the neighboring veins and arteries should not?

Classification of thymus cases by various observers can be summed up in the following grouping:

A. Status Thymus (No changes in lymphatics).
  1. Simple hyperplasia with clinical and anatomical evidences of compression.
  2. Simple hyperplasia without any symptoms.
  3. With an accompanying increased activity of the thyroid which may cause clinical symptoms of exophthalmic goitre.

B. Status Thymo-Lymphaticus.
  1. Enlarged thymus associated with general enlargement of lymph tissue like adenoids, tonsils, spleen and mesenteric glands.

To both groups may be added congenital enlargement of the thymus and lymph glands. Cases of congenital thymus enlargement have been reported by Heidinger, Kayser, Somma and others, but the question has been raised by some as to their being true cases of this condition. Crotti suggests that asphyxia neonatorum may possibly be due to congenital thymus hyperplasia.

Hammar has done pioneer work in disproving the old ideas as to thymic death. His has been the most reliable work performed, as all his experiments, observations and deductions were carried out with mathematical accuracy and precision. He claims that thymic death is not of thymus origin and he seems to have proved his case. The thymus in cases of sudden death from internal causes differs in no respects from thymus in healthy children. He compared the microscopic findings in 16 children from 3 weeks to 15 months old and analyzed and compared them with an equal number from apparently well children killed by accident or dying from external causes. He arrived at the following conclusions: (1) The two so-called critical spaces are so near together that they can be considered as one, particularly in the new born. (2) The statement that the trachea is greatly compressed immediately before the bifurcation where the innominate artery crosses is erroneous, for the innominate artery lies above the bifurcation. If the trachea was actuallly compressed at that point by the thymus, that part of the thymus lying immediately opposite, just above the base of the heart, must have been responsible. (3) Since the thickest portion of the thymus lies at the level of the base of the heart, just below the critical point, drawing the thymus upward would intensify dyspnea, since it would bring the thicker mass of the thymus between the top of the sternum and the spine. It would not relieve dyspnea produced by pressure of the thymus on the trachea. (4) If ascent of the thymus relieved inspiratory dyspnea, it was proof that the point of compression of the trachea did not lie above the thickest part of the thymus, but at, or below the thickest portion in the neighborhood of the bifurcation. The thymus is not forced upward into the neck with each inspiration but recedes into the thorax; it is forced up into the base of the neck during expiration, so that if it produced dyspnea by compression of the trachea, it would produce it during expiration and not during inspiration.

Hammar proved that the notions of mechanical compression of the trachea by the enlarged thymus are largely false. His anatomical preparations show that an enlarged thymus may exert pressure close to the bifurcation or on the bronchi, particularly in the new born, but he does not say that it actually does.

He also disproved that enlargement of the thymus is constant in thymic death. He showed that it was not possible to distinguish any fixed type; in fact, in the majority of glands, variations were within the normal limits. He studied 14 cases, 13 of which were in children (ranging in age from 9 days to 16 years). He estimated the exact amount of parenchyma, minus the fat and connective tissue, by serial sections and reconstruction and in the same manner determined the exact relation of the medullary to the cortical substance. He counted the number of Hassal's corpuscles. He found that of the 13 children, the thymuses of only two were enlarged, while the others showed amounts of parenchyma that were within the normal limits. The cortical medullary index was high (normal). He arrived at the conclusion that no morphological ground exists on which to rest a theory of hypofunction or dysfunction.

Other Theories of Thymus Death

Tracy advances the view that there is a superabundance of "Hormone X" in the blood stream and insufficiency of adrenin. The existence of Hormone X has not been substantiated.

N. Paton believes that thymus death is a pluriglandular syndrome and that in the absence of secretions of these glands and because of general imperfect development, death is more easily produced by trauma which would otherwise be ineffectual.

McNeal says that "status lymphaticus is an abnormal condition in the body in which if anaphylactic phenomena occur, they do so in an exaggerated way." He advances the theory that it is an intensified anaphylactic condition but produces no proof.

Wooley, with others, thinks that the clinical phenomena are due to over-functioning of the thymus. There has not been any supporting evidence to warrant this conclusion.

Another theory that has not been substantiated is one that tries to explain the symptoms as end results of an intoxication from the products of a faulty metabolism.

Symptoms of Enlarged Thymus

Enlargement of the thymus may cause no symptoms at all and the first warning of the presence of the condition may be a sudden paroxysm of severe dyspnea which may or may not terminate fatally, or else there is a sudden death from some slight cause or following a trivial operation. The chief complaint is nearly always a cough or attacks of choking which come and go, frequently in paroxysms. Friedlander calls attention to three definite symptoms, i. e., dyspnea, stridor and suffocative attacks with cyanosis. The dyspnea is the most striking sign and may be constant or intermittent with or without paroxysms. The stridor is inspiratory in character, and may be aggravated by fits of anger, exertion or sudden retraction of the head; it is more marked in sleep because of the position of dorsal decubitus assumed.

Diagnosis of Enlarged Thymus

Diagnosis of this condition depends upon physical examination and X-Ray examination. While some clinicians question the possibility of making a positive diagnosis of a normal thymus by means of percussion, there have been many who have been able to demonstrate an enlargement by this method. A favorite with many is the so-called "Threshold method." The child is placed on his back in the mother's lap. Percussion is begun well out in the chest, with such light strokes that when the ear is within a few inches of the area under percussion only the faintest possible resonance is heard. When sound disappears, dullness begins. Some observers outline the borders of dullness by the tactile sense of resistance rather than sound. The outer limits are determined much more easily than the lower boundary. This latter, which may be obtained by auscultatory percussion, is relatively less important. The percussion outlines, determined in this way, according to Benjamin and Lange, correspond remarkably closely to the Roentgenograms. A clinical diagnosis of thymic enlargement is never absolutely positive without X-Ray confirmation.

Friedlander was the first to treat this condition fully by the X-Rays. His first case has since had an anesthetic and has been operated without any bad results. He summarizes the treatment as follows: (1) In the X-Ray we have an agent which is at the same time safe and efficacious in the treatment of enlarged thymus and status lymphaticus. (2) It is possible to induce not only an involution of the thymus, but also in cases of status lymphaticus, to reduce the size of the spleen, of the lymph nodes and to change the lymphatic picture to a normal one. (3) The dosage of the X-Ray can be regulated according to the necessities of the case. Where the symptoms of thymic asthma are urgent, the exposures can be given on successive days. A thymus partially involuted by the X-Rays is capable of regeneration. The shadow of the normal thymus occupies a V-shaped area which scarcely extends beyond the limits of the median bony structures. An enlarged thymus gives a wide median shadow above the heart appearing like a broad cap superimposed on the shadow of the heart and great vessels. This shadow is suggestive of thymic enlargement when it extends for some distance on either side of the bony structure, above the heart shadow and continuous with it.

Cook advises that children with retarded mental development, if suspicion is directed toward the thymus, should have the thymus rayed. In the so-called lymphatic type of children, he suggests thymus raying as a pre-operative procedure.

Operative Procedures

Immediate operation should be performed in children if the mechanical symptoms are alarming. Tracheotomy may be of avail. The operation most frequently done now is that of thymectomy, the earlier ones of exothymopexy and resection of the upper part of the sternum having been to a great measure discarded.

Organotherapy

Rational organotherapy is at present impossible owing to very unsatisfactory knowledge of the gland and its functions. None of the diseases in which thymus treatment has been tried has been shown to be related to either thymus hypofunction or dysfunction. As Sajous has shown, if any results attend its administration, they are probably due to the high nucleic content of the thymus. It has been used for cretinism and hypothyroidism in conjunction with thyroid for the possible effect on the osseous development. This relationship between the bony system and the thymus must be cleared up before this empiric treatment can be given a scientific basis. It is used also in rickets, Addison's disease, infantilism and osteoarthritis. Sajous advises it in the condition known as progeria, a premature senility in which the child attains senility in a few years; he thinks the condition is due to deficient activity of the thymus.

Hanaborg recently advocated its use in chorea, having obtained good results in 16 cases of this disease. He thinks it plausible to assume that acute articular rheumatism may so affect the thymus that the secreting function is impaired and the unstable nervous system of the child feels the lack of the normal restraining influence of the thymus. Thymus extract seems to have a sedative effect on the nervous system. It controls convulsions, these recurring when the treatment was suspended. Thymus insufficiency, in his opinion, may be an added factor to the infection, but he gives salicylates in addition.

Hanaborg's work awaits confirmation.

The Science of the Future.— Dr. Eulogio Perez.

All persons of average culture, among others, physicians, understand, although imperfectly, that all maladies may be effectually resisted by the organism itself, which fights and defends itself energetically against an enemy which we little comprehend, in spite of all our microscopes, and with weapons not well defined or known, but which are so real and effective that their action is evidenced if we merely recall the innumerable spontaneous cures of this scourge of humanity called tuberculosis.

In our own organism we discover the true panacea; for as Nature creates our enemies, it also creates the opposing substances in order to maintain organic equilibrium.

Our scientific work in the future, as regards therapeutics, will undergo such a radical transformation that, of the old, will remain only that which might be temporarily efficacious, and the greater needs will be met with the series of active glandular elements, the true regulators of health, which modern science is beginning to know, although amidst the greatest obscurity and confusion.

Brief Abstracts

Alkali Treatment Applied to the Acidosis of Epidemic Influenza.— Thomas C. Ely, M. D., (*New York Medical Journal*, April 5, 1919).

Epidemic influenza is a concrete instance of acidosis. The remarks in this article are applicable to all toxic conditions in which acidosis occurs. Acidosis demands the immediate and persistent use of measures of elimination and alkalies.

Acidosis is a constant factor in all infectious fevers and in the recent influenzal epidemic the acidosis was particularly prominent. Infection from streptococci and other pyogenic organisms are always attended by marked acidosis and in the present epidemic these were especially in evidence. Clinical evidence of this was the acetone breath, dyspnea and air hunger. The therapeutic proof was most convincing — administration of sodium, potassium and calcium was immediately followed by the gradual cessation of acidosis symptoms.

In addition to influenza cases, cases of pneumonia, pregnancy and intestinal infection have been treated with a large percentage of recoveries by the alkaline treatment.

Starling tells us that, "In abnormal cell metabolism the first, middle or last stages of oxidation may be at fault, generally the last stages fail of complete oxidation, acidosis results, and acid poisons are formed. The alkalescence (electrical neutrality) of the fluid media of the body is a necessary condition for the continuance of the life of the cells and especially of the normal processes of oxidation. It is therefore essential for the preservation of life that the acids thus formed and accumulated as a result of impaired oxidation processes, should be neutralized, carried to the kidneys and excreted by them in combination with some base. When these acids are produced in large quantities, the alkalies, sodium, potassium, and calcium of the food and of the tissues, do not suffice for their neutralization. Ammonia, which is a constant intermediate stage in the production of urea, is then utilized for this purpose."

Physiology then teaches that if the relative proportions of acids which have to be eliminated from the body are short of necessary bases, sodium, potassium and calcium from food and tissues, and short of ammonium; if these alkaline reserves have been withdrawn and used, the poison acids cannot be neutralized and life cannot be preserved unless these bases are supplied. The reason for the success of elimination and alkaline treatment and the benefit of supplying to the body from without, these harmless alkalies, sodium, potassium, and calcium, becomes apparent. * * *

When ammonium and the fixed bases, sodium, potassium and calcium, are more or less exhausted in the neutralization of acids, symptoms of acidosis or acid intoxication result. However, such a result is usually prevented by the abundance of ammonium. Unfortunately, if ammonia does not suffice, and the sodium, potassium, and calcium salts of the tissue juice do not suffice and are not furnished from without, the condition of acidosis is serious and fatal. It is a simple matter and an entirely scientific procedure to furnish these alkaline bases from without and prevent the serious and often fatal acidosis. * * *

Obviously the correct therapeutic measure is not to administer an alkali of one type, as sodium bicarbonate, but a mixture of sodium, potassium and calcium, in order that all these may be present in abundance in the tissues and the equilibrium of the fixed alkaline bases in the central nervous system be thus maintained.

"To give simply soda, is little better than the body offers, which is ammonia only. The results of alkali therapy are more certain if all the alkaline bases are administered." * * *

Taylor adds that, "An acidosis that draws largely upon the firmly combined cations (sodium, potassium and calcium) in the tissues must ultimately be dangerous. The law of mass action demands that it is impossible to conceive of acid of the body combining with ammonia alone, but under all circumstances there must be some abstraction of sodium, potassium and calcium from the tissues. Long continued acidosis must lead to the dangerous abstraction of alkalies from the tissues."

The corollary of the necessity of supplying these alkaline bases is axiomatic and a highly scientific procedure, founded on facts of physiology, pathology, and physiological chemistry. And a free water supply must be essential to carry on with advantage the laws of osmosis with these bases of different weights, combining with poison acids through the system. Elimination of the combined products must be equally essential. Too much alkali might produce an alkalosis and prove harmful, and it seems the best judgment to keep within the limits of moderate alkaline dosage. For the same reason the use of sodium and alkalies should be under the guarded care of physicians, and its use promiscuously by the public is to be condemned for fear of producing harmful alkalosis. * * *

Immediate elimination is instituted by profuse sweating and divided doses of calomel, one tenth grain every half hour until a grain or more has been given. Water exclusively is given for the first twenty-four or forty-eight hours, and water is also given freely by mouth or by bowel throughout the attack. Sweating is preferably accomplished by drinking large bowls of hot boneset tea. Janeway, of New York, in the early epidemics, preferred large bowls of boneset tea to all other diaphoretics. My experience has been that nothing else equals it in value. Hot lemonade with whiskey was often given. Hot mustard foot baths were always used, the patient being kept in bed covered with blankets and surrounded by hot bottles. I have always explained to the patient that immediate pain relieving remedies do not tend toward recovery, but prevent elimination of poisonous products or depress the heart. However, with the elimination and alkali saturation the severe pain is usually controlled in a short time.

At the outset and through the attack, I gave every patient the three well known alkaline substances, sodium bicarbonate, potassium citrate, and the calcium salts in the form of lime water. To every patient I administered a teaspoonful of sodium bicarbonate to a pint of luke warm water every four hours by enema. In routine treatment I have given this simple prescription to spare the overworked druggist: Sodium bicarbonate one half ounce, peppermint water four ounces; teaspoonful every two hours, alternating with potassium citrate one half ounce, peppermint water four ounces; teaspoonful every two hours. The calcium salts I gave in the form of lime water one third, milk two thirds. * * *

In addition, I have employed the common cardiac and respiratory stimulants, strychnine, caffeine, spartein, digitalis, camphorated oil, oxygen, and aromatic spirits of ammonia. I have found oil of terebinth useful, particularly after crises. It is an efficient stimulant, a valuable antiseptic and penetrates the whole system. In many cases of faulty elimination, I have found dry cupping a valuable adjunct. In all cases the patient was confined to bed, and the use of a bedpan was made imperative. * * *

An Experimental Investigation on Rickets. — Edward Mellanby, M. A., M. D., (*The Lancet*, March 15, 1919).

It is but little realized how great and how widespread is the part played by rickets in civilized communities. The bony deformities occur only in a small part of the cases affected. Schmorl's investigations on children dying before the age of four showed that 90% had had rickets. Lawson Dick found 80% of the children in the London County Council Schools had rickets. Defective teeth are commonly associated with rickets. The reduced resistance to other diseases of the rachitic child is so marked that the causative factor of rickets may be the secret of immunity or non-immunity to many children's diseases.

The experimental work on puppies described in this investigation has shown that the animal's whole behavior may be changed in the early stages. Such animals show a low resistance. In the author's investigations more than 200 puppies were used. The experiments have clearly shown that, though there may be other factors the dietetic problem is the primary key to the problem. In the experiments no special type of dog was used, although it is realized that the susceptibility of different breeds varies greatly. Methods used to detect rickets have depended on (1) X-Ray examination, (2) calcium estimation of the bones after death, (3) histological preparations of the bones.

The puppies were started on their diets after leaving the mother, the ages varying between 5 and 8 weeks, the latter being the more usual. They were kept for varying periods according to the type of experiments. In the earlier periods they were usually killed after five to six months, but as the work progressed and the diet became more rachitic this time was considerably shortened.

Having obtained diets which normally produce rickets, various substances were added and the effect on the development of the disease noted. Using diet I (175 cc whole milk per diem, porridge, equal parts oatmeal and rice and ½ gram NaCl) increasing the whole milk to 500 cc prevents rickets. On diet II, meat and extracts of meat have an inhibitory effect, while the protein after loss of the extraction allows rickets to develop. The addition of most fats prevented rickets. Yeast has no protective influence. The results of these diets are shown in the following table:

TABLE I. — RACHITIC DIETS

Diet I	Diet II	Diet III	Diet IV
Whole milk, 175 c.cm.	Whole milk, 175 c.cm.	Separated milk, 175 c.cm.	Separated milk, 250-350 c.cm.
Oatmeal, rice, 1-2 g. NaCl	Bread ad lib.	Bread (70 per cent. wheaten) ad lib.	Bread (70 per cent. wheaten) ad lib.
		Linseed oil, 10 c.cm.	Linseed oil, 5-15 c.cm.
		Yeast, 10 g. NaCl, 1-2 g.	Yeast, 5-10 g.
			Orange juice, 3 c.cm.
			NaCl, 1-2 g.

TABLE II. — DIET I PLUS MORE WHOLE MILK

Diet	Duration Months	Histology Results
Diet I	4	Rickets
Diet I	8	Rickets
Diet I	7½	Rickets
+ 325 c.cm. milk	5	Normal
+ 325 c.cm. milk	5	Normal

TABLE III. — DIET II PLUS MEAT AND MEAT EXTRACTS

Diet II	4	Rickets
+ dog biscuit	5½	Rickets
+ dog biscuit	5½	Rickets
+ water ext. of meat	4	Normal
+ meat protein	5	Rickets
+ 80% alc. ext. of meat	5	Normal
+ 10 g. meat	5½	Normal

TABLE IV. — DIET II PLUS YEAST AND MALT EXTRACT

Diet II	5½	Rickets
+ 10-20 g. yeast	5½	Rickets
+ 10-20 g. yeast	5½	Rickets
+ malt ext.	4	Normal
+ malt ext.	7	Slight rickets

TABLE V. — DIET II PLUS DIFFERENT FATS

Diet II	4	Rickets
+ 10-20 g. butter	6	Normal
+ 10 c.cm. codliver oil	9	Normal
+ 10 c.cm. linseed oil	5	Rickets
+ 10 c.cm. linseed oil	5	Rickets
+ 10 c.cm. peanut	5½	Normal
+ Water ext. of butter	6	Rickets

TABLE VI. — DIET III WITH VARIOUS FATS INSTEAD OF LINSEED OIL

Diet III	3	Rickets
Diet III	3	Rickets
	Weeks	
With codliver oil	17	Normal
With butter	17	Normal
With olive oil	17	Slight rickets
With peanut	17	Slight rickets
Diet III	17	Rickets

When a patient is run down, has failing strength, prostration after exercise, cold hands and feet, with perhaps anemia, constipation, want of attention to business affairs, weakness of memory, weak will power, inability to perform mental work, incapacity of decision and other symptoms that are associated with a run down condition, it may be confidently asserted that the function of the dynamic glands of internal secretion is below par.

This condition may be more or less persistent or may occur at intervals, just as almost all of the constitutional psychoses are dominated by a periodicity. There may in fact, be a melancholia of the body just as there is a melancholia of the mind. In these cases physical effort is almost impossible; there is a well defined physiologic laziness. Such conditions as these afford a fine field for pluriglandular therapy.

Hormotone is a preparation that imparts the necessary physiologic "kick" for such cases. Patients take on a new lease of life. They sleep better, eat better, in many cases their constipation is overcome, and they get a feeling of self confidence that enables them to battle anew with the problems of every day life. Hormotone institutes and maintains normal function of the suprarenals and the glands associated with them, the thyroid, pituitary and the gonads. These glands form what has been termed the adrenal system and they furnish to the blood what have been very properly termed the dynamogenic hormones. Run down conditions and the lowering of mental and physical virility are accompanied by, and are probably due to, a deficiency of these hormones. Thus a perfect hormone balance is essential to the maintenance of health and to the restoration of a run down condition. Hormotone provides it. — Advertisement.

TABLE VII. — DIET III PLUS MEAT AND MEAT EXTRACTS

Diet III + 5 g. meat	17	Rickets
+ 20 g. meat	17	Rickets
+ 50 g. meat	17	Rickets
+ water ext. of 50 g. meat	12	Rickets

An examination of the results suggests that rickets is a deficiency disease.

Of the three factors known, fat-soluble A, water-soluble B, and antiscorbutic, two of these can be at once excluded. Yeast has no preventive influence on the development of the disease, and in consequence water-soluble B cannot be considered as of importance. Again, orange juice, sufficient to exclude any possibility of scurvy when considered with the rest of the diet, did not inhibit the disease, and this therefore allows the exclusion of the antiscorbutic factor. On the other hand, the anti-rachitic substances for the most part have been found, so far as the rickets experiments have gone, to be similar to those in which, according to the experiments on growth, of McCollum, Osborne, Mendel, and others, fat-soluble A is present. It therefore seems probable that the cause of rickets is a diminished intake of an anti-rachitic factor which is either fat-soluble A, or has a somewhat similar distribution to fat-soluble A. The facts are not at all in favor of this hypothesis as it stands, and these will be discussed in the next lecture.

Substances which had no preventive action were separated milk, bread, meat protein, yeast, linseed oil and hydrogenated fats. Those with well marked preventive action were cod liver oil, butter and suet. Those of less marked action were meat meat extract, malt extract, lard, arachis, olive oils.

The results seemed to favor the hypothesis that experimental rickets can be prevented by diets containing an abundance of anti-rachitic factor and that the anti-rachitic factor and fat-soluble A have somewhat similar distributions.

Relation of Rapidity of Growth to Development of Rickets.

Rickets develops best in rapidly growing animals, this fact being in harmony with the clinical observation that large and rapidly growing children most often suffer from rickets, whereas marasmic children generally escape. It is, therefore, difficult at first sight to associate a disease of rapid growth with a deficiency of fat-soluble A which is, according to accepted teaching, necessary for growth. I think, however, that it can be definitely stated that the amount of growth a puppy experiences has no relation to the amount of fat-soluble A in the diet, although a small minimum amount may be necessary.

It has, however, been already pointed out in this work that large and rapidly growing puppies require more anti-rachitic factor to prevent the development of rickets. If, therefore, fat-soluble A and the anti-rachitic factor are identical the presumption is that the function of fat-soluble A in the diet of puppies is not so much to ensure growth as to promote correct growth; in other words, to keep the growth straight, and the greater the amount of growth in any period the greater is the amount of fat-soluble A necessary to keep it along normal lines. If this view is correct, then it can hardly be claimed that fat-soluble A is in any different category from the point of view of growth than the antiscorbutic factor; for, even in the absence of this latter, the rate of growth diminishes and there is often rapid loss of weight.

The Action of Meat and Meat Extracts.

The second difficulty involved in considering the anti-rachitic factor and fat-soluble A as identical is the part which meat and meat extracts play in the development of rickets. It has been seen that, although when added to Diet II these substances prevent rickets, in the case of Diet III rickets develop. Yet even in the Diet III and IV experiments, the action of meat is undoubtedly inhibitory in nature and, when 50 gr. of meat are given, will almost prevent rickets in a small puppy. It is probable that the anti-rachitic action of meat may therefore be due more to its making the fires burn more brightly, and thereby increasing the effectiveness of any fat-soluble A present in the body, rather than to the fat-soluble A it possesses in itself. If this explanation of the action of meat be true, then it is still possible to regard fat-soluble A and the anti-rachitic factor as identical.

Whether the anti-rachitic factor is fat-soluble A as previously understood is therefore undecided, but, on the whole, these substances appear to be identical. It is at least certain that the distribution of the two substances is remarkably similar.

REVIEW OF SOME EARLIER HYPOTHESES AS TO ETIOLOGY

Dietetic Hypothesis — Rickets as a Disease due to Deficiency of Fat. — Development of rickets does not depend on fat per se but rather on the type of fat and whether it contains an abundance of the anti-rachitic factor.

Excess of Carbohydrate in Diet. — Diets of cereals transformed in manufacturing processes are most deficient in anti-rachitic factor and are effective in producing rickets.

Deficiency of Fat and Excess of Carbohydrate. — This condition comprises the first two.

Deficiency of Calcium Salts in the Diet. — It is probable that a deficient calcium intake associated with deficient anti-rachitic factor will bring about a more acute production of rickets.

The "Domestication" Theory of Rickets. — Von Hansemann's "theory of domestication" includes in a comprehensive way all the unhygienic conditions associated with life in civilized and more particularly in crowded communities.

Effects of Confinement. — Exercise must give a greater opportunity to any anti-rachitic factor in the food economy. My own experience is that confinement will not produce any symptoms of rickets in adequately fed puppies.

GENERAL CONSIDERATION OF RICKETS AS A DEFICIENCY DISEASE

It will be noticed that, although rickets has been interpreted on the basis of my experimental results as primarily a deficiency disease of a dietetic nature, this has not prevented other conditions from receiving attention and being considered as of some importance. A knowledge of general metabolism would not allow the exclusion of other factors; for dietetic problems must always be regarded as a whole, and the idea that accessory food factors can be considered separate and apart from other elements of the diet and from the general metabolism is unsound.

An adequate diet is itself a unit, and its soundness, to a large extent, consists of the mutual assistance and interplay in the metabolic changes the elements experience in the body. The absence of, or deficiency in, one element means the ineffectiveness of another. For instance, the absence of carbohydrate involves a defective oxidation of fat, and probably an inefficienct protein metabolism. Similarly, it is possible to imagine an abundance of accessory food factors in the diet which may, however, be ineffective because of some wrong balance in the energy-bearing materials. The same argument applies where the metabolism varies for reasons other than diet.

These few words are all the more necessary because recent work on accessory food factors has appeared too self-contained and, if persisted in, may be responsible for a period of disbelief in their existence with subsequent lack of progress in the study of a subject which is obviously of prime importance both from the academic and practical points of view.

It appears, then, from this work that the foodstuffs of an infant ought to contain a maximum amount of anti-rachitic factor. Since, further, the dietetic problem is one of balance, foodstuffs which contain no anti-rachitic factor cannot be considered as neutral, but as positively rickets-producing, for the more of them that is eaten the greater is the necessity for foods containing the factor. Since there is a limit to what a child can eat, the inference is obvious. It is probable that bread is the worst offender, and to allow bread to form too large a part of an infant's dietary seems to me to be courting disaster. The same statement may apply to other cereals, but this has not been worked out to any extent.

Another point of importance is the type and amount of fat eaten by children. Since the above

In the treatment of intestinal indigestion and constipation no medicament is equal to that furnished by organotherapy. Duodenal extract, in the form of secretogen, stimulates the production of secretin, the master key that unlocks the storehouses of the digestive secretions.

The treatment of these conditions with Secretogen differs radically from the old-time measures in that the physician does not have to sentence the patient to the use of it for the term of his natural life. Secretogen is really restorative — not merely palliative. Secretogen promotes the flow of bile, of the succus entericus, the pancreatic ferments, and, incidentally, will relieve most cases of constipation to an extent that will astonish the physician. It will thus be seen to be of very great value in cases of toxemia arising from intestinal putrefaction. On the other hand where putrefaction has gone to such an extent that diarrhea is present, with its accompanying foul-smelling stools, the use of Secretogen will bring back formed stools and normal movements.

The most prolific cause of intestinal putrefaction is enzyme deficiency and in intestinal indigestion, whether or not accompanied by intestinal stasis, Secretogen has no peer. Prescribed in suitable cases it makes a grateful patient. — Advertisement.

remark as to the limited amount of food a child can eat applies with even greater force to fat, it is necessary to give children the best fat from the point of view under consideration. They should therefore not be given vegetable margarines or any other vegetable fat. The natural fat for a child is the fat of milk, and to give it a vegetable fat not only limits the amount of butter it can eat, even if procurable, but also weighs down the diet in the rachitic direction.

If additional fat is given to that normally eaten, then cod-liver oil is the best.

Milk as an Anti-rachitic Factor.

Undoubtedly milk ought to remain the staple article of diet not only until weaning, but for some years after this time. Milk is undoubtedly better than the corresponding amount of butter. Under normal circumstances the child would then be assured of a good supply of anti-rachitic factor.

Studies on Alimentary Hyperglycemia and Glycosuria. — C. V. Bailey, M. D. (*Archives of Internal Medicine*, April 15, 1919).

The present work was undertaken in an attempt to show the relation of glycosuria to hyperglycemia as found in health and as influenced by disease. Experiments were conducted on a normal person and in cases of early and long standing renal diabetes, diabetes without kidney involvement, chronic interstitial nephritis, hyperthyroidism, myxedema, hypopituitarism, dyspituitarism and parenchymatous nephritis.

In the normal person the results seem to indicate that when uninfluenced by food or fluid intake, reducing substances are present in equal concentration in both blood and urine. Following the ingestion of glucose, urine sugar parallels that of the blood up to the latter's concentration of 0.16 to 0.17 per cent. As the blood sugar increases beyond this point the kidneys actively excrete sugar. This excessive excretion decreases as the hyperglycemia passes off. There seems to be an attempt to control the blood sugar concentration by an increase in blood volume. This is partly brought about by a decrease in urinary excretion.

SUMMARY

In the series of cases reported one finds variations in the blood sugar value after fifteen hours' fasting. Normal values are found in cases of renal diabetes, early mild diabetes, hyperthyroidism, hypothyroidism, hypopituitarism, dyspituitarism, and in a normal case. High blood sugar values are found in cases of nephritis, and diabetes of long standing with or without renal involvement. In the synchronous urine specimens two only showed the presence of glucose by Benedict's test. One was from a patient with a blood sugar of 0.098 per cent. whose kidneys at that time were excreting glucose at the rate of 2 gm. per hour. The other case showed a constant glycosuria of 0.5 per cent. independent of the diet.

In the twenty-four-hour urine specimens, glucose was found in the cases of renal diabetes, early mild diabetes, diabetes with and without renal involvement, hyperthyroidism, and chronic parenchymatous nephritis with constant glycosuria.

CONCLUSIONS

1. Sugar is a constant constituent of normal urine, and, during a fasting and thirsting state, the concentration in the urine approximates that in the blood.
2. Following the administration of small amounts of glucose (30 gm. or less) the blood sugar increases, and its demonstration depends entirely on the frequency of the estimations.
3. In a normal person the sugar in the urine parallels that in the blood up to the latter's concentration of 0.16 to 0.17 per cent. Above that the kidneys actively excrete sugar. In returning to the normal value the decrease in blood sugar precedes that in the urine.
4. Alimentary hyperglycemia in uncomplicated diabetes is characterized by a rapid rise and fall.
5. When diabetes is complicated by renal involvement, alimentary hyperglycemia is prolonged.
6. Alimentary hyperglycemia is prolonged in myxedema and hypopituitarism.
7. In nephritis alimentary hyperglycemia is delayed and prolonged.
8. The concentration of blood sugar at which glycuresis occurs varies in different individuals, and is influenced by disease, being abnormally low in early diabetes, high in diabetes of long standing, in nephritis, and in deficiency of the thyroid or hypophysis.
9. Glycuresis is a kidney function and is excessive in diabetes and hyperthyroidism. It is greatly decreased in nephritis and in deficiency of the thyroid or hypophysis.
10. Blood sugar estimations one hour after the ingestion of glucose may be the same in renal diabetes, early diabetes, or normal cases.
11. Blood sugar estimations two hours and three hours after the ingestion of glucose may be the same in diabetes of long standing, in nephritis, myxedema, or in hypopituitarism.
12. Blood volume increases with the development of a hyperglycemia, returning to normal with the blood sugar.
13. Blood sugar is about equally divided between plasma and corpuscles.
14. Sugar in the corpuscles increases in proportion to that in the plasma.
15. Excretion of sugar is uninfluenced by the rate of urinary excretion, excepting in some cases of parenchymatous nephritis.
16. Morning blood sugar estimations are of great diagnostic value. The urine excreted at the same time should be tested for sugar and the rate of excretion determined. As the morning blood sugar varies under treatment, diagnostic tests should be made after the patient has been on regular diet for several days.

17. Tests of alimentary hyperglycemia are of little clinical value; especially is this true of tests made at one hour intervals.

18. Examination of the twenty-four-hour urine for sugar (Benedict's new method), or better, fractional examinations, detects cases of excessive glycuresis.

19. Test of alimentary gylcuresis following the ingestion of glucose (100 gm. for a person of average weight, that is, 1.7 gm. per kilogram) is a valuable diagnostic and prognostic method, the urine sugar being estimated at frequent intervals for the succeeding six hours, and the total excretion determined. This, in conjunction with the morning blood and synchronous urine sugar estimation, probably tells us as much about the case as do the elaborate tests herein reported.

A Simple Urine Test for Acidosis, Clifford Mitchell, M. D., Chicago, Illinois, (*Medical Record*, March 8, 1919).

Titration of the acidity of the urine is not a reliable procedure for the determination of acidosis. Other factors enter into the acidity of the urine. Acetone bodies in urine indicate acidosis but diacetic acid is the only one readily detected by simple chemical tests and in this determination many fallacies may occur. The determination of the carbon dioxide content of the alveolar air requires special apparatus and may not be available in smaller communities, and the conjoint examination of the blood and urine is hardly suited to the routine practice of medicine.

The writer has devised a simple trustworthy urine test, accomplished without the need of special apparatus, special skill or chemicals. This has been used successfully in the case of two types of acidosis, — diabetes mellitus and that of pernicious vomiting of pregnancy. The foundation of the test rests upon the fact that urine has the property of decolorizing iodine in solution in potassium iodide solution.

The best way to apply the test, so far discovered, is the following: to 145 c.c. of water (hydrant water will do) are added 3 c.c. of Lugol's solution and 2 c.c. of a saturated solution of picric acid, the whole being thoroughly mixed. The result is a fine clear, reddish liquid of bright color. Pour this liquid into a white dish and heat it. The writer heats it on the water bath to a temperature of 180 F., but if a water bath is not available it may be heated over the flame until fumes are abundantly given off, boiling being avoided by turning down the flame sufficiently. When thus heated, the urine is added as quickly as possible but in small amounts at a time, the writer using for this purpose a graduated burette. If, however, a burette is not available, a small graduate or graduated bottle may be used from which to pour the urine into the hot liquid. It will be found that in acidosis the amount of urine needed to turn the bright red color to a bright yellow color is small, and the smaller the worse the case. In

The view that diabetes is an incurable disease is giving way. That it is a "disorder of nutrition" (Osler), has long been recognized because it is always preceded by intestinal indigestion due to pancreatic insufficiency. It is also known that the inability to utilize carbohydrates is due to derangement of the internal secretion mechanism of the pancreas. Physicians are beginning to realize the truth of von Strumpell's dictum, "To treat by diet only is not to treat at all."

A Massachusetts physician, in the Boston Medical and Surgical Journal says: "My experience in the use of drugs or special remedies with the exception of one preparation, is unsatisfactory. The continued and intelligent use of Trypsogen in certain selected cases of a pancreatic type seems to have a beneficial influence." He cites five cases in four of which Trypsogen rendered excellent service.

Trypsogen is the first thought of many physicians when they get a fresh case of diabetes; and that often because it was the last thought in the first case in which they used it.

Keep Trypsogen in mind when you get your next case. — Advertisement.

severe cases 2 or 3 c.c. of urine will almost immediately discharge the red color. In cases of moderate severity 8 or 10 c.c. may be required. Normal urines do not usually affect the color in smaller amounts than 15 c.c., except possibly in unusual conditions of concentration, where the amount of urine in 24 hours may be but a few hundred cubic centimeters. In most cases of normal urine, of specific gravity ranging from 1,015 to 1,020, the amount of urine required to effect change from red to yellow is around 20 c.c. or even higher, as high as 50 c.c. in some cases.

There is no trouble about the end reaction in this process as the mixture remains fairly clear, sometimes entirely clear. If the change from red to yellow is not easily recognized, it will be of avail to have near by in another white dish about 150 c.c. of a saturated picric acid solution for purposes of comparison. With practice the titration can be made so closely as to repeat within a fraction of a c.c., provided a constant temperature is kept and if the process is rapidly performed.

If from day to day the color is discharged by less and less urine, the case is growing worse. If, on the other hand, more and more urine is daily required to turn the red to yellow, the patient is improving.

Theories Regarding Blood Pressure.—Harold W. Dana, (*Jour. A. M. A.*, May 17, 1919).

Recently studies were made of a large number of army officers and candidates for commission in the army. The greater number came a considerable distance and were examined the day after arrival without opportunity for rest. Most of them were nervous and constipated. A large percentage showed elevation of the systolic blood pressure. In a great majority of such cases, however, rest, catharsis, and the fact of becoming accustomed to the new routine of life, soon brought the blood pressure down to within normal limits. It served to demonstrate in a very striking way the effect of overwork, nervous strain, psychic stimulation, and constipation, in raising blood pressure. Familial hypertension was encountered with great frequency. Such a condition of continued elevated systolic pressure, in which most members of particular families share, the tendency apparently being hereditary, does not seem in such families to cause invalidism or to shorten life.

Such a condition shakes our faith in any preconceived standard for normal systolic pressures. These familial hypertension cases as a general thing, can be accepted as representing to all intents, and for that particular family, a condition free from serious organic disease. Another type in which there is difficulty in setting down a standard for normal blood pressure is the case in which the hypertension is compensatory to renal or arterial disease. In this general category come those cases in men of 50 years or over in which the blood pressure has assumed a probably normal and physiologic elevation. Taken by and large, our conception as to what represents an unduly high systolic blood pressure in a given individual must take a good many facts into consideration, must be highly individualized, and must have considerable latitude, both as to the standard accepted and the interpretation to be placed on deviation from the standard.

It does not seem that marked hypertension necessarily causes apoplexy or predisposes to apoplexy or of renal or arterial disease. A considerable proportion of men with sclerosis of the peripheral vessels have a normal blood pressure and in a similar proportion of cases of hypertension there are soft radial arteries.

We have accepted certain standards from the pioneers of sphygmomanometry and there has been little opportunity for exact observation correlating physiology and pathology along this line and it seems that most of the supposed facts of blood pressure that we accept are still open to proof and subject to doubt.

Dana's argument is, that the systolic blood pressure is maintained by vasoconstricting substances in the circulating blood, and that an abnormally high blood pressure indicates that the blood stream contains either toxic substance (whether unexcreted products of metabolism or of focal purulent processes) or an excessive amount of the vasoconstricting secretion of particular glands of internal secretion. The functional test of cardiac efficiency suggested by the observation of Graupner that when a man has been put through a certain amount of exercise, and when following this his pulse rate has returned to normal, his systolic blood pressure as a rule rises, would seem to me to be better explained by the theory that there was an increase in the amount of vasoconstricting internal secretion, liberated perhaps by the thyroid or suprarenal glands as a result of the increased circulation following exercise, rather than on the basis of the condition of the heart muscle.

He believes, as do many others, that a systolic blood pressure of 150 or 160 mm. may be normal for a man 50 years old. To his mind, the ratio 2:3 for the diastolic and systolic pressures, respectively, should be maintained by the normal heart regardless of the rise or fall of pressure; and with a pressure of 160 mm. systolic, he believes that an intact circulation would show a diastolic pressure of from 105 to 110 mm. The relatively lowered diastolic pressure in thyrotoxicosis and in "effort syndrome" may perhaps be explained either as a vice of internal secretion, or perhaps in the case of "effort syndrome," as the result of intestinal stasis.

CONCLUSIONS

1. It is believed that increased systolic blood pressures indicate the presence in the circulating blood either of unexcreted putrefactive products absorbed from the intestine, from the kidneys, from focal infections in the dental alveoli, the nasal

sinuses, the tonsils, the genito-urinary tract, or of secretions in abnormal amounts from the glands of internal secretion.

2. It is believed that in some cases at least, a lowered systolic blood pressure indicates a defective secretion of pressor substances, or an increased secretion of depressor substances by the ductless glands.

3. It is believed that the diastolic pressure, when it fails to conform to its normal ratio with the systolic pressure, is also influenced by abnormal products of metabolism or by abnormal amounts of ductless gland secretion in the blood stream.

4. It is not believed that either the systolic or the diastolic blood pressure gives any certain indication as to the condition of the cardiovascular renal system as such; and that when changes in the vascular system are accompanied by hypertension, neither condition is secondary to the other, both being held to be secondary to the presence of unexcreted toxic products of metabolism in the circulating blood.

Asthma as a Digestive Symptom-Complex.—Mark I. Knapp, (*Medical Council*, Nov., 1918).

The correctness of the theory of the origin of asthma as expounded in this article is confirmed by a successful practice in over three hundred cases. Asthma as at present understood, is faulty in the conception of its etiology and pathology and chaotic in the application of therapeutic media. The cause of asthma was suggested by the results obtained in the treatment of four cases of insufficientia pylori complicated by asthma. In each case the cure of the stomach condition was attended by the cure of the asthma. This led to the conclusion that there must be a certain and definite and intimate relationship between insufficientia pylori and asthma.

Insufficientia pylori is defined as non-closure of the pylorus; the pylorus offering no resistance to the ingested food from escaping from the stomach into the intestine in an undigested condition. As the ingested food failed to undergo action by the gastric juice, the ingesta leaves the stomach unprepared for intestinal digestion. Abnormal chemical reactions with excessive gas formation takes place in the intestine and physical distension of the abdomen results. This pressure, equal of course in all directions, presses against the diaphragm and causes compression of the thoracic viscera, the heart and the lungs. The interference with the normal function of the lungs due to this great resistance results in suffering which is expressed by the symptom complex we call asthma. After the digestive disturbance was corrected the lungs were permitted to expand normally.

As to cardiac or renal asthma the author says that no adequate proof can be given or has ever been given of the causative relationship between these diseases and asthma and that in both renal and cardiac diseases the digestive functions suffer. It is a question whether the concomitant asthma

Success in the treatment of tuberculosis depends upon improving nutrition and raising and increasing the resisting powers of the organism. The best antiseptic for diseased tissue is a healthy blood plasma, and, in addition to good food, fresh air and rest, great aid can be rendered to the tuberculous patient by appropriate organotherapy.

Dr. Leonard Williams says: "By the use of vaccine therapy we may repel an individual invasion, but we have done less than nothing so to fortify him (the patient) that out of his own resources he will in future be able to resist successfully similar onslaughts."

The point is well taken. No tuberculin or serum administered in tuberculosis, however useful it may be in combating the immediate condition, carries with it those physiologic elements which will enable nature to repair her shattered bulwarks. Repair and recovery can come only through the organism itself.

Subsequent to the use of Kinazyme, a rapid improvement is observed in the constructive metabolism of the body, as shown by an increase in weight and strength. Kinazyme is a therapeutic adjunct to the hygienic routine in tuberculosis and gives the most satisfactory results in the majority of cases. By its use a larger amount of food is digested and absorbed and the resisting powers of the organism are greatly increased.

Try Kinazyme in some case of tuberculosis. Your patient will know the difference.—Advertisement.

is due to the disturbed function of the alimentary canal or to the heart and kidneys.

Of the assumption that nasal conditions cause asthma, the author says that one third of his cases came to him after they had gone through one or more nasal operations; had the sufferers been cured of their asthma, they would not have come to him. That asthma is not "Nervous" the author illustrates by a 6 mos. old baby that was sent to him by one of his cured asthma cases. Instead of the baby the mother was treated and the baby recovered from its asthma.

The prognosis is excellent. Abatement of symptoms may begin within 36-48 hours. The patient should be impressed with the fact that asthma is a condition which depends upon the digestion and the diet.

The treatment is of the underlying insufficiency of the pylorus and requires alkalies. The degree of the insufficiency must be ascertained so as to know how soon after the meals the alkalies are to be given. This is done by repeated test meals given on succeeding days, each day waiting 15 minutes less for the aspiration of the test meal. Alkalies are administered only when we know the stomach to be empty. The chief alkalies are sodium bicarbonate, magnesium oxide and calcium carbonate. These may have to be augmented by citrate or acetate of potash, sodium or ammonium chloride or ammonium carbonate. Frequently cascara must be added. An initial dose of castor oil is frequently of benefit. Colchicum seems to be of value. Strychnin, hyoscyamin, and atropin are of great service and should be used according to indication. The constant use of adrenalin is warned against and potassium iodid is stated to be inferior to ammonium iodid. For checking the asthmatic paroxysm the author advises quickly emptying the stomach and the bowel by lavage of the stomach and enema.

Concerning the diet, tea, coffee, cocoa, beer, wine and effervescent drinks must be excluded; distilled liquors if necessary, should be diluted. The varieties of vegetables and meats to be allowed must be studied in each case. As the patient improves the diet list is to be lengthened but this must be done with great caution. The patient must be watched daily for a period of from two to three weeks, during which time a few changes both in diet and therapy will be found necessary. Perseverance, persistence and patience are the requisites to cure the unfortunate asthmatic patients.

Phenol with Hydrogen Peroxid for Local Applications.*

Referring to Dr. Soresi's article, (Journal of the A. M. A., May 3, 1919) Miró states that if crystallizable phenol (full strength) is applied with brush or swab to the surface of the skin or mucous membrane, a whitish spot results, followed by local anesthesia. This method can be used for many operations; will cure light infections as ingrowing toe nails, furuncles, acne, etc. Crystallizable phenol is suggested since that liquefied by the addition of alcohol or glycerin does not produce such an intense blanching.

If the white spot is touched with undiluted hydrogen peroxid it will not disappear if the tissues are normal; "if the submucous or subepidermic tissues have suffered alterations, the white spot will darken until it becomes black, and the nearer to the surface the affected tissues lie the darker it will become. This black spot is in reality a scar which can be opened slowly, since it is anesthesized, and the incision will surely open a way for the pus, debris, etc. It is a splendid method of diagnosis, prognosis and treatment."

This method may be followed in the case of furuncles, gummas, ulcerations, gum abscesses, suppurating hematoceles, tonsil abscesses, and Velpeau's syphilitic chancre.

In suppurating bubo phenol is followed by peroxid, then by incision, evacuation of pus, drying, packing with phenol soaked cotton and then by cotton soaked in peroxid.

Transplantation of Thyroid with Intact Blood Supply.

— K. Kawamura, (*Jour. Experimental Medicine*, July, 1919).

Thyroid transplantation through blood vessel sutures was accomplished by Kawamura. This method was selected because of the restoration of the circulation of the gland. The dogs used in the experiments showed that the thyroid which was transplanted by means of various methods of blood vessel anastomosis showed good growth and function for several months despite the interference with the circulation for some hours. The circulation through the blood vessels thus transplanted was satisfactory, but the experiments indicate that such transplantation is not permanently successful.

Fat Redistribution in the Hypophyseal Type of Dystrophy Adiposogenitalis.

— Harvey G. Beck, (*American Journal of the Medical Sciences*, November, 1918).

The function of the pituitary, like that of the thyroid, presides largely over growth, development and metabolism. The gonads also have an important influence over growth and development, but perhaps somewhat less over metabolism. There is a close reciprocal function between these three glands which has been observed clinically and demonstrated experimentally.

Because of this reciprocal function, true hypophyseal fat dystrophies are rather rare. On the other hand the mixed or pluriglandular types are quite common. It is not uncommon to find in the same individual clinical evidence of hypothyroidism, hypopituitarism and hypogonadism in which the character of dystrophy varies, depending upon the relative insufficiency of the respective glands.

---

* Abstract of a letter from Dr. A. Péréz Miró, Havana, *Journal A. M. A.*, June 14, 1919.

Although primary genital dystrophy occurs, it is relatively infrequent as compared with hypophyseal dystrophy. Moreover, the genital type usually early becomes a mixed type, in which hypophyseal symptoms predominate.

In the study of a large series of cases of hypothyroidism, fully 20 per cent. showed marked evidence of hypophyseal fat dystrophy, and practically all the female patients, which comprise nearly the whole group, gave a history of ovarian deficiency.

Disordered function of the pituitary gives rise to various types of dystrophy, depending on overfunctioning-hyperpituitarism; underfunctioning-hypopituitarism; or perverted functioning-dyspituitarism.

Gigantism and acromegaly are generally ascribed to a hyperfunction of the anterior lobe, although recently Roussey's doctrine, according to which it is due to dyspituitarism, has received many adherents. The dystrophies in these conditions are largely confined to cartilage and bone.

It is generally conceded that the fat dystrophies of pituitary origin, with which we are chiefly concerned in this paper, are due to hyposecretion of the posterior lobe. The most commonly recognized form is known as hypophyseal dystrophy adiposogenitalis-typus Frölich, by whom it was described in 1901.

The pathogenesis of adiposis dolorosa, or Dercum's disease, has not been definitely established, although it is undoubtedly a ductless glandular disease, possibly pluriglandular, in which the posterior lobe of the pituitary shares in a very large measure.

The adiposity that is frequently associated with acromegaly is thought to be due to secondary involvement of the posterior lobe.

A number of cases of hypophyseal dystrophy are described. Case I female, 41 years of age, married, never pregnant, weight 125 lbs., height 5 ft. 3 ins. Weight had increased 20 lbs. in the 10 mos. preceding examination. There was enormous increase in the circumference of the hips, upper thighs and abdomen, but not of the thorax, neck, arms, face, hands, or feet. These appeared emaciated. There was also apathy, stupor, dullness, impairment of memory, sluggish movement and trophic disturbances. Three fairly well-defined symptom groups were recognized in this case, namely, those referable to ovarian unsufficiency, sterility and amenorrhea; those referable to pituitary insufficiency — abnormal character and distribution of fat; those referable to thyroid insufficiency — mental, neuromuscular and trophic skin disturbances.

On the basis of a pluriglandular syndrome, *hormotone*, which contains the substance of the three glands involved, was prescribed. Four tablets, with the addition of two grains of thyroid, were given daily. The results were very striking. The patient was speedily restored to normal mental and bodily vigor and was able to perform her usual domestic duties without the least fatigue; but the most remarkable effect of treatment was upon the fat dystrophy, the so-called dystrophia adiposogenitalis, as evidenced by a rapid diminution in the circumference of the hips and abdomen. Thyroid was discontinued on June 14, but she continued to take four *hormotone* tablets daily until July 15, after which glandular therapy was discontinued. Since then, a period of two years, she has had no return of symptoms and retained her normal figure.

In case II the woman, aged 49, weighed 148 lbs. One year previous to examination she began to suffer with pain in the back, painful and frequent micturition, polyuria, headaches, emotional disturbances and mental depression. Never pregnant. Her figure was abnormal, being relatively twice as large from the waist down as from the waist up. Her waist measurement was 69½ circumference and the hips 113 circumference. After one month's treatment with hormotone and anterior pituitary lobe she lost 2½ lbs. and her general condition had much improved. The result of organotherapy in these cases was pronounced. Although but 2½ lbs. of weight were lost the patient had to have her skirts reduced around the hips three times. The results clearly demonstrated that in a certain group, possibly 50 per cent., there is a redistribution of fat rather than a loss of fat.

Chronic focal infection and trauma through surgical intervention to some of the chain of ductless glands, especially the thyroid and sexual glands, are fairly constant factors in the history of patients suffering with dystrophy adiposogenitalis, and may have an important etiological significance.

In case III a woman aged 42, weight 118 lbs., suffered from chronic appendicitis for 6 years. During the year previous she developed symptoms of hypothyroidism, mental dullness, loss of memory, somnolence, muscular and joint pains, subnormal temperature and exhaustion. Large cushions of fat accumulated about her hips and upper thighs. The fat extended down to the middle of the thigh and over the gluteal region and above the ilii. There was also a big fold of fat over the lower abdomen, with enlargement of the mons veneris, presenting a typical picture of dystrophy adiposogenitalis.

The treatment consisted of the removal of the appendix and administration of thyroid and anterior pituitary lobe. This had a remarkable influence upon the shape of the body. The general improvement compares favorably with the restoration to her normal shape with a gain of three pounds in weight.

Other cases of this type, similarly treated, have demonstrated the fact that the fat is redistributed and that the mere weight of the patient is no criterion on which to base the results of treatment. The influence of organotherapy can best be determined by mensuration.

In none of the cases was any special attention paid to diet. The obesity is endogenous.

BOSTON MEDICAL LIBRARY AUG 27 1920

Book Reviews

The Newer Knowledge of Nutrition, The use of Foods for the Preservation of Vitality and Health. — By E. V. McCollum, School of Hygiene and Public Health, The Johns Hopkins University. Cloth, Price $1.50, Pp. 199, Macmillan Co., N.Y. 1919.

This book presents the subject matter of the Thomas Clarence Cutter Lectures delivered by the author at Harvard Medical School. In addition to an interpretation of the current literature on nutrition it gives the results of the authors own experiments in the "deficiency diseases," and in a remarkably concise form describes the modern conception of dietary requirements. The systematic experiments and logical deductions with reference to the etiology of scurvy, pellagra and rickets carry conviction and give a better understanding of these diseases. The book gives a comprehensive survey of the "Vitamine Hypothesis" and of the numerous researches in this new phase of the science of nutrition. The author's criticism of the term "vitamine" has much to commend it but it is doubtful if the term Fat Soluble A and Water Soluble B will replace it in literature. After full consideration of McCollum's criticism the term "vitamine" still seems to be a very acceptable name. A comprehensive bibliography is appended.

The care, choice of method, attention to detail, elimination of sources of error, and introduction of methods of precision shown by the author should serve as an example of true scientific method in biology. The book should be read not only by students of nutrition but by every medical practitioner.

An Introduction to Neurology. — By Judson C. Herrick, Professor of Neurology in the University of Chicago. Second edition 1918, cloth, 351 pages, W. B. Saunders Co., Philadelphia.

This work is the very best presentation of the subject from the standpoint of pure science that has come to the reviewer's attention.

The campaign for increased requirements in pre-medical instruction has laid special emphasis on physics, chemistry and biology with the result that the medical student today as a rule, presents adequate qualifications on his entrance to the medical school.

It can be safely said that none of these subjects is of more importance to the medical student than general neurology presented in the manner so well done in this text book. Sound conception of the theory of medicine, clinical pathology and general physiology can result only from an adequate understanding of the structure and function of the nervous system.

This little work is not only logically and splendidly arranged but it also offers a correction for a pedagogical error in most works on the subject. It presents structure in relation to function. The schematic plates are excellent and the absence of elaborate plates for the demonstration of structure is explained by the author's statement that the work is not intended to supplant the more exhaustive atlases or take the place of the actual dissection.

The book should be read by every medical student, and the college student planning extended work in psychology, zoology or general physiology should find it of the greatest value.

Internal Secretions and the Nervous System. — By Dr. M. Laignel-Lavastine, Nervous and Mental Disease Publishing Co., New York and Washington, 1919. Authorized translation by Dr. F. T. Robeson, N. Y., paper, 75c.

It is difficult to conceive of a work of the size of this volume that contains so much substantial and practical matter in the field of endocrinology. The extremely important relation between the organs of internal secretion and the vegetative nervous system is clearly set forth.

The author, Dr. M. Laignel-Lavastine, shows that in pathology there are two classes of disorders; first, nervous disorders in the endocrine syndromes, and second, endocrine disorders in the nervous syndromes. In the first case the primary disturbance is in the nervous system, and in the second instance in the endocrine system. The vegetative nervous system is made up of two parts, the sympathetic and the autonomic. Some of the internal secretions act on the one, other secretions act on the other. The experiments quoted from Eppinger and Hess show this by aid of pharmaco-dynamic tests by the injection of adrenalin, pilocarpin, and atropin. They have given the name of vagotonics to individuals in whom activities of the autonomic predominate and sympathicotonics to individuals in whom the sympathetic excels.

The discussions of neurological and endocrinological investigation and the critique of these methods is well written. In his critical comment and search for sources of error in the methods used, the author inspires confidence, and his whole method of approach is one that should be emulated as a good example of the application of true scientific methods to problems in a field of knowledge which has, up to the present time, been largely built upon unproved assumptions. In addition to the theoretical matters considered, the book has a decidedly practical application in the well written sections on nervous disorders depending on endocrine glands.

The discussion of what are termed "ordinary symptoms," asthenia, headaches, insomnia, anxiety, sweats, constipation, arterial hypertension, and obesity is also of decided value to the general practitioner as an aid to diagnosis and the recognition of the part that disturbance of the endocrine glands plays in these commonly observed symptoms.

The work of the translator, Dr. F. T. Robeson, has been exceedingly satisfactory and his preface well states the problems under discussion.

M.E.C.
...TON MED...
FEB 20
LIBRARY
552

English Edition 195,000

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

Vol. IV **1919** **No. 3**

CONTENTS

Suprarenal Therapy 51
Acidosis 53
The Placenta and Its Therapy 55
Antiscorbutics 57
Albuminuria in Pregnancy 58
The Discovery of Thyroxin 58
Fever and the Water Reserve 59
Suprarenal Cortex Therapy 60
Groping in Medicine 61
The Pathogenesis of Cancer 62
Diagnosis of Incipient Tuberculosis 63
Rational Treatment of Neurasthenia 64
Hypothyroidism in Women 66
The Treatment of Gastric Ulcer 66
Hysterectomy in Ovarian Function 67
Addison's Disease & Sergent's White Line 68
Corpus Luteum in Neurological Practice . . 68
The Function of Chromaphil Tissue 68
The Nutritive Value of Yeast 69

High Blood Pressure II
Digestive Disorders III
Tuberculosis, Kinazyme in IV
Hormotone Without Post-Pituitary V
Diabetes Mellitus VI
Monoglandular Products VII
Menstrual and Menopausal Disorders VIII

HORMOTONE

Blair Bell says: "A woman is a woman on account of the sum total of her internal secretions." The truth of this aphorism is soon realized by the physician who uses **Hormotone** in

MENSTRUAL AND MENOPAUSAL DISORDERS

In menopausal conditions associated with hypertension use
Hormotone Without Post-Pituitary

Dose of either preparation: One or two tablets three times daily.

LITERATURE ON REQUEST.

G. W. CARNRICK CO. **13-15 Laight St., New York**

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

Vol. IV **1919** **No. 3**

Suprarenal Therapy

THE suprarenals are among the chief factors in the *entente cordiale* that obtains among the glands of internal secretion in a normal physiology and as such they shoulder a heavy responsibility. Engaged as they are in the development of the glands that play the major part in the perpetuation of the species and also engaged in a strenuous role as the chief protagonists in maintaining the dynamic force of the body, the physiological importance of the suprarenals is constantly in evidence.

The suprarenals and the therapy of their substances are now much better known than they were a few years ago. The most active principle of the medullary portion of the gland is in use everywhere and to larger purpose. The hastily conceived notions of its unavailability for use by mouth administration reached the waste basket long ago. Suprarenin is now employed locally, hypodermatically, intravenously and by mouth. Dentists and nose and throat specialists use it every day and its oral administration is a frequent occurrence in internal medicine.

It is probable, however, that the field for its employment in the future will be almost exclusively as a topical application. In this domain it stands alone.

In surgical practice the official 1-1,000 solution of adrenalin diluted 100 times so as to get a concentration of 1 in 100,000 has been used in promoting the healing of wounds. The wound is irrigated and packed with gauze dipped in the solution. The healing is said to be hastened in a remarkable degree, the wound filling in with granulation tissue until it reaches the surface.

As an internal medication the use of epinephrin or even the desiccated medullary portion of the gland is giving way to that of posterior pituitary substance or its active principle. Posterior pituitary is less dangerous and more lasting in its effects than epinephrin and is rapidly ousting it in the treatment of acute conditions requiring immediate relief. This does not apply, however, to cases where there is definite involvement of the suprarenal glands as the incriminating factor in diseased conditions. In these, suprarenal therapy, exemplified by the exhibition of the whole gland substance or that of the cortex, will always hold a place, and when there is evidence of organic change in the glands no other organotherapeutic measures can be used as substitutes for them.

In the treatment of pellagra whole suprarenal substance has been used. A French physician reports that in his opinion, pellagra is the result of defective function of the endocrine glands, especially the suprarenals. The sympathetic system suffers in consequence and this in itself might cause many of the symptoms of pellagra. Three cases of pellagra that he treated with suprarenal therapy apparently sustain his assumption, as two of the patients recovered completely under systematic suprarenal treatment. The third patient succumbed to a concomitant liver abscess, and the suprarenals were found twice their normal size, hard and purple in color.

In vomiting of pregnancy whole suprarenal substance has also been used. Sergent thinks that the suprarenals are a means of defense in the control of the toxemias arising from the pregnant condition. He has noted that where this toxemia is extremely well marked, the suprarenals may become rapidly exhausted through the call made upon them to combat it. He has treated refractory vomiting with suprarenal substance and records several cases in which prompt results were had from cachets containing five grains of substance given two or three times a day.

In cardiac disorders accompanied by weakness, especially where there is dilatation, cyanosis or edema, suprarenal therapy has been employed to advantage. Sajous explains the benefit of suprarenal preparations in cardiac adynamia in that the suprarenal secretion contributes to the heart's working power in two ways: (1) By enhancing directly the contractile power of its right ventricle; and (2) By sustaining oxidation and metabolism of the entire cardiac muscle. Mankowsky says that its efficacy is best shown in cardiac weakness and threatening collapse. Floersheim states that when powdered suprarenal substance is placed on the tongue, mixed with saliva and masticated thoroughly its effects appear within ten seconds. At other times it takes ten minutes to regulate a weak, irregular pulse, but the usual time has been between two or three minutes.

Contraindications: Sajous says that these are mainly: chronic nephritis, aortic lesions with tendency to anginal pains, angina pectoris and arteriosclerosis, in all of which conditions a marked increase of the vascular tension would be harmful.

Suprarenal therapy then is pre-eminently homostimulative and homonutritive and most authorities agree that absolute preference should be given to its employment by mouth in the form of desiccated whole gland substance or desiccated cortex.

The whole gland has been used with success in many other disorders, mainly as a substitutive measure in suprarenal hypoplasia. Here it is given much the same as thyroid in myxedema and in fairly large doses, 8 or 9 grains daily

Addison's Disease: Among other conditions in which suprarenal substance has proved advantageous may be mentioned Addison's disease. Sajous says that the dose should be adjusted to the needs of each patient. Beginning with three grains of the desiccated extract three times daily after meals, the dose should be gradually increased until the temperature and the blood pressure become normal, when the last dose should be maintained. However, the opinion seems to be veering that this disorder is more nearly related to a lesion of the cortex than of the medullary portion of the gland, and one or two observers have reported extremely gratifying results by the exhibition of cortical substance.

Suprarenal therapy has also been employed with more or less success in the treatment of osteomalacia, rickets, tuberculosis and asthma.

In the treatment of hypoadrenia accompanying typhoid and other fevers, it has been used with success. In many instances the daily dose has been too small. Once sure of the diagnosis of hypoadrenia as instanced by Sergent's white line, whole suprarenal substance, orally administered, may be safely given in the daily dose mentioned, split up into small portions frequently repeated. The tiny dose by itself has a too transitory effect. Given often, so as to keep the patient constantly under the influence of the medication with due regard to the daily maximum required, the patient is brought into a condition of suprarenal equilibrium and the best therapeutic effects are obtained. This, of course, applies to the hypoadrenia of such disorders as cholera, typhoid and the exhaustive fevers generally, and is not so applicable to the persistent use of suprarenal substance in chronic suprarenal insufficiency. Here the desiccated whole gland may be safely given in two or three grain doses two or three times daily.

Chronic asthenic conditions generally are benefited by such doses but it will be found that pluriglandular therapy is, in the long run, superior to the employment of suprarenal substance alone in such cases. In these chronic run down conditions more than one gland is involved and the best results have followed the use of a combination of tiny doses of such glands as the thyroid, pituitary and gonads.

Influenza: Indeed, many of these so-called cases of suprarenal hypofunction or dysfunction are essentially pluriglandular in their origin. Lately there has been some discussion of the asthenia and low blood pressure accompanying influenza and influenzal pneumonia. Necropsy reports have revealed hypoplasia of the suprarenals in these cases and the belief that they are involved is further strengthened by a characteristic rise in blood pressure following the prolonged administration of epinephrin. However, those conducting the observations are of the opinion that if epinephrin is of any use in the treatment of the symptoms of suprarenal dysfunction the proper method of administering it seems not yet to have been found, as there is an absence of the normal leucocyte response to the subcutaneous injection of epinephrin in these conditions. If pluriglandular therapy had been employed in these cases it would have been noted that not only was there a rise in blood pressure after the administration of a suitable combination of gland substances, but that the exhibition of them gave rise to a distinct leucocytosis. Moreover, where pluriglandular therapy is employed the differential count is not disturbed as it often is when giving a simple, gland product such as thyroid, for instance, alone. Pluriglandular therapy in the asthenia due to influenza and influenzal pneumonia has given excellent results, much better indeed than when a monoglandular product has been employed.*

That gastric ulcers have followed removal of the suprarenals has been known for some time and this has led to the employment of suprarenal therapy, not only in the treatment of ulcers but in the treatment of other gastric conditions. Some of the later studies in internal secretion have developed a relationship between the digestive tract and the endocrine system. Gastric ulcer is usually associated with the suprarenals while that of the duodenum is associated with the thyroid.

Cortex Therapy: In the light of these observations the importance of the article on suprarenal cortex therapy in this issue of THE METABOLIST, indicating that it is the cortex that is at fault and that cortex therapy is beneficial in the treatment of gastric ulcer, is not to be lightly estimated. It is, of course, far from the last word in the treatment of lesions of the digestive tract by organotherapy but the results attained by the author in his treatment of gastric ulcer surely blazon the way to more important developments in the future study of gastro-enterological conditions and their treatment.

Acidosis

ACIDOSIS is perhaps the most indefinite term introduced into scientific medical literature within recent years. The term as originally proposed by Naunyn in 1906 was intended to apply to that pathologic condition in which beta-hydroxy butyric acid is formed. Later, with the extension of the term to other conditions, it has been proposed to designate that special form of acidosis, characterized by the appearance of the acetone bodies, (diacetic acid, hydroxy butyric acid, and acetone), as ketosis. This is the type commonly found in diabetes. At the present time the tendency is to define acidosis as a depletion of the "alkaline reserve" of the body. Acidosis is an unfortunate term, for as stated by Bayliss (*British Med. Jour.*, Oct. 5, 1918), if it means anything it implies that the blood becomes acid, and a survey of the literature makes it clear that the term "acidosis" is not reserved for "acid reaction" of the blood. Increase in the hydrogen ion concentration is a terminal stage of acidosis; it occurs only when the normal equilibrium between acids and bases in the body is disturbed and the physiological protective system completely broken down, such as occurs in diabetic coma.

The alkalinity of the blood is maintained with remarkable constancy within narrow limits in the normal body. When measured by the hydrogen electrode or selected indicators the reaction is practically the same as water. A hydrogen ion concentration sufficient to give a color change with methyl orange would be incompatible with life.

The neutrality of the blood is maintained principally by an interesting equilibrium maintained by the salts of the blood and corpuscles and to less extent by the proteins. This "buffer action" of the blood refers to its property of being able to take up considerable quantities of acid without appreciable change in the hydrogen ion concentration. In the plasma itself the bicarbonates are the all-important salts. The normal constant ratio of H_2CO_3: $NaHCO_3$ is 1:20. When acid of any kind is added it reacts with the bicarbonate to form a salt and H_2CO_3. The hydrogen ion concentration resulting will not increase in proportion to the amount added in the acid for the reason that H_2CO_3 is but slightly dissociated, but the slight increase is promptly removed by the lungs as CO_2, the removal of CO_2 permitting the hydrogen to react with the remaining atom of oxygen to form water, and again restore the 1:20 ratio of H_2CO_3: $NaHCO_3$.

The H ion is the normal stimulus to the respiratory center so that any increase causes increased respiratory efforts and this accounts for the hyperpnoea common in acidosis. When the bicarbonate is no longer sufficient in amount to maintain the neutrality in cases of continued addition of acid the phosphates may enter into reaction, the di sodium phosphate being converted to mono sodium phosphate, or acid phosphate which is excreted by the kidneys. If even this mechanism is insufficient there may be an altered nitrogen metabolism and ammonia diverted for the neutralization of acid and excretion in the urine. Free acid itself may be excreted. Protein may combine with free acid, but this is probably much less efficient in maintaining neutrality. It will be seen from an examination of this mechanism that there may be a marked diminution in the alkali reserve of the body without an increase in H ion concentration. So long as the 1:20 ratio is maintained, the acidosis is said to be "compensated." Here the absolute value of the alkali may be diminished but the H_2CO_3 is also diminished. Only when this ratio is altered is it said to be uncompensated.

---

* See advertising page.

Diagnosis: The actual determination of the H ion concentration of the blood is neither easily made nor of great value. "Since it is only in severe acidosis that changes occur in the reaction of the plasma as it exists in the body, the measurement of the reaction, the hydrogen ion concentration, is a measure of the excitability of the respiratory center rather than the degree of acidosis." (W. McK. Marriott, *Archives of Internal Medicine*, 1916.)

Possibly the capacity of the blood to absorb CO_2 from an atmosphere of CO_2 at a given constant pressure is the most accurate and satisfactory measure of acidosis. Whole venous blood should be used with a constant partial pressure and the results give not only the bicarbonate reduction but the total alkaline reserve of the body (phosphates, etc.)

Since the equilibrium between the dissolved CO_2 of the blood and the CO_2 in the alveoli is in accord with the gas laws, it follows that determination of alveolar CO_2 gives a means of determination of the acid-base ratio in the blood. In acidosis the CO_2 of the blood is reduced, hence alveoli CO_2 tension is reduced. Aside from certain factors other than mere H ion concentration, which affects this alveolar tension, the technical difficulties in making such analyses do not make it a practical method.

It has been noted above that the kidney plays an active part in eliminating acid substances from the blood and various urinary tests for acidosis are based upon this. The total acidity of the urine may be determined by titration with standard alkali ($\frac{N}{10}$NaOH) using sulpho phenolphthalein or phenolphthalein as indicator. To this must be added the total amount of ammonia in the urine. Results of determining total acidity of the urine show consonance with the results obtained from the method using the CO_2 combining power as its basis.

Much less accurate methods for bedside work are the determination of acetone in the urine by the nitro prussiate test and of diacetic acid by ferric chloride.

For the general practitioner the tolerance to alkali is a most accurate diagnostic procedure for acidosis. In normal individuals, *i.e.*, in persons with normal alkali reserves, the administration of over approximately 5 grams sodium bicarbonate per day will render the urine alkaline. In acidosis it may require as much as 100 grams per day to make an alkaline urine. The test is simply performed and should be made as a matter of routine practice.

Causes: Acidosis is not a primary condition. It is not *per se* a disease. It is a pathologic (usually) state characteristic of many diseases. It occurs physiologically in change of altitude. It may be found in diabetes, nephritis, vomiting of pregnancy, starvation, gas poisoning, suppurative processes, following anesthesia, etc. Increase of acids in the plasma is always evidence of faulty oxidation. Without adequate oxygen supply and great muscular work lactic acid is the end product instead of CO_2. In the absence of carbohydrates the complete oxidation of fats does not take place and partially oxidized fatty acids (oxybutyric and diacetic, etc.) accumulate. Starling (*Human Physiology*, page 895) says: "The condition of acidosis however, is often brought on directly as the result of putting the patient on a strict anti-diabetic diet, *i.e.*, one consisting chiefly or exclusively of fats and proteins, and may be produced in a healthy man by simple starvation, when the body has only at its disposal its stored up fats and proteins. It occurs in a marked degree on the administration of a diet consisting almost entirely of fats. Thus in one experiment a healthy man took as his sole diet for five days a daily ration of 250 grams of butter, 200 grams of oil, and a little wine. The result was an intense acidosis such as is only found in the severest cases of diabetes, diacetic acid, oxybutyric acid and acetone being found in the urine in large quantities." Acidosis may result from failure of the kidney to eliminate acid bodies with the consequent accumulation in the body. In nephritis, acidosis is due to this cause and is not uncommon.

Treatment: Alkali, particularly sodium bicarbonate may be administered and forms an important part of all treatment. The effort should be made to bring the alkali reserve to its normal value but never exceed it. It may be given by mouth or intravenously. Just enough should be given to bring the reaction of the urine to normal. Indiscriminate use of alkalies is dangerous. The salts formed as a result must be eliminated and if the kidney is not properly functioning these salts may be retained and create a grave condition in the body. The diet should be reduced, particularly fats and proteins. Free diuresis must be maintained. A carbohydrate diet is useful and glucose may be administered. Glucose has a large percentage of oxygen in its molecule and in its metabolism a large percentage is set free for other oxidations. Thus for the formation of one molecule of stearic acid, three molecules of glucose are required with a splitting off of 16 atoms of oxygen (Starling, *Human Physiology*, page 888). In urgent cases a 4% or 5% solution may be given intravenously. Free diuresis should be maintained and water in as large quantities as can be tolerated should be given. Glucose is valuable for this purpose also as it acts as a diuretic. The proper regulation of the diet is essential. Meat except possibly in small quantities should be avoided, and fats should be reduced to very small quantities. Skimmed milk may be given or lime in milk. Purgation is sometimes indicated and in cases of deficient renal function may afford prompt relief.

The Placenta and its Therapy

THE fact that all lower animals, wild and domestic, have an instinct impelling the mother, immediately after delivery, to eat the placenta, suggests an important field for the therapeutic administration of this gland to the parturient woman. This instinct for eating the placenta, found universally in animals, persists still in certain savage races.

The observation of the animal instinct of placentaphagia combined with the fact that history and tradition show no more ancient and more nearly universal opotherapy than this, suggests that there are excellent reasons for the administration of desiccated placenta by mouth in suitable cases.

The important therapeutic value of the placenta may be realized when it is recalled that it is rich in nucleins, oxyhemoglobins, ferments and hormones, as would be expected in an active temporary organ.

Many experiments have been carried out with the placenta to determine its physiological activity. Physiologically the placenta has a great variety of functions besides the obvious one of a filter for the body fluids of mother and child. It is equipped to perform all manner of metabolic processes, resembling in this respect the intestines, liver, pancreas and even the spleen. Most important of all are the hormones of the placenta which promote the growth of the unborn child while they prepare for its future nutrition by developing the breasts. The placenta too, through action of its hormones, promotes the involution of the postpartum uterus as well as the growth of the gravid uterus through pregnancy.

The fact that the placenta acts through the mediation of a hormone in the blood and not through nerve connections is clearly proved by the uterine reaction, normal in all details, which occurs when the gestation is ectopic.

The activating power of the placenta is independent of the influence of the ovaries. The placenta causes normal hypertrophy of the glandular tissues of the breasts and induces lactation as well as hypertrophy of the entire uterus, even after the ovaries have been removed. Ribbert in 1897 found that transplanted breasts secreted milk after labor.

Frank found that placental extract caused hypertrophy of transplanted portions of the uterus, as well as of the uterus in situ. This action is not diminished by removal of the adrenals, pancreas or thyroid, or combined removal of thyroid and adrenals.

Experimentation has shown that, in the placental lipoids there is contained a hormone which in its action, chemical and biological, resembles very closely a similar hormone of the corpus luteum. This hormone is very slightly soluble in water, and is completely soluble in 95% alcohol.

The production of a placenta depends upon (1) the sensitization of the uterus for eight or nine days after ovulation by the special substance produced by the corpus luteum. (2) A mechanical stimulus supplied by the presence of the ovum. Any number of placentæ may be produced artificially in the rabbit and guinea pig. The uterus is artificially sensitized by corpus luteum, mechanical stimulation of the endometrium is made artificially and the placenta develops. Even in transplanted uterine tissue this phenomenon occurs provided it is not attempted from one individual to another (Loeb 1909). It is thus again shown that nerve influence is not necessary for placental development.

The effects of administration of placenta by the mouth or intravenously are congestion and hypertrophy of all the uterine tissues and hypertrophy of the mammary glands. If the milk flow occurs, placenta administration increases the quantity and quality of the milk. The placenta does not initiate the milk flow. Although the placenta does not produce milk, it stimulates the growth of the parenchyma of the mammary gland furnishing more and better cells which produce more and better milk.

The uterine activity resulting from placenta administration has led to the employment of placenta in uterine diseases, infection, hypertrophy, malnutrition and subinvolution. The explanation of how the placenta improves these conditions is that the pathological conditions are overcome by the increased blood supply brought to the uterus and the consequent hypertrophy of the tissues through the agency of the placenta hormone.

The literature on this subject shows that almost all cases of deficient flow or deficiency of constituents of the milk have been benefited by placenta administration. This is shown by the rapidly increased weight of the infants and the residual milk often left after nursing. Because of the fact that domestic animals devoured their placentæ immediately on their appearance, Van Hoosen, 1915, gave 30 to 50 grains desiccated cow placenta in divided doses to some women during the first twelve hours after parturition. The first report was a complaint by the nurses that the mother had so much milk that "it was a burden to keep the breasts empty." On one day six of the mothers nursed their babies allowing them to take all they would, and a total of 44 oz. of surplus milk had to be removed by the breast pump. In one case there were 16 oz. extra, in three others 6 oz. each, and in a fifth, 8 oz., and in the remaining case, 4 oz. The initial loss of weight by the infants was reduced and the later gain was increased by this feeding of placenta.

The value of placental tissue as a galactagogue is also endorsed by Cornell, 1918. He says that 87% of the babies whose mothers had received dried cow placental tissue began to gain by the fourth or fifth day, as against 69% whose mothers did not receive this medication. 44% regained their birth weight before leaving the hospital against 24% who did not. Cornell found that the most satisfactory dose was 5 grains three times a day for twelve doses. The first dose was given immediately after labor. Cornell reported more than 100 cases besides 70 controls. They left the hospital by the ninth day. 13% supplied milk to other babies.

Bouchacourt published several favorable results. In one case the milk was increased from 90 to 380 grams after the administration of 20 grains of placental extract. Another was increased from 100 to 200 grams. After a daily dose of 10 grams of extract of placenta, one case with the daily quantity of milk only 40 grams increased to 275 grams, then 300 grams and finally 470 grams.

For uterine hypertrophies and subinvolution as well as for retarded uterine development, the doses of placenta indicated are smaller but are continued for a longer time.

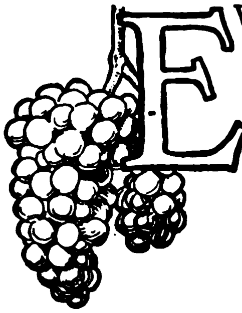
Other Indications: Anticipated or actual deficient milk supply either in quantity or quality. Subinvolution of uterus and infantile uterus, also presence of chronic uterine infection.

Dose: For a galactagogue placenta is administered in divided doses commencing at the middle of pregnancy or at any time when a deficiency of the milk quantity or quality is noted, and continued until the flow of milk is satisfactory. Daily doses may vary from 10 to 40 grains. No objectionable features have been noted with larger doses. Dosage for improvement of uterine conditions is 3 to 5 grains three or four times a day.

The placenta is one of the most recent additions to our list of endocrinic glands. In the literature on the subject of placental administration, there is fortunately, less contradiction in the results of observers than was usual in experimental work on the other endocrines. The slight contradictory results of some authors can be easily explained by the varying strength and condition of the extracts and preparations employed. Fortunately, there seems to be no maximum dose; poisonous action of the properly prepared placenta has never been observed.

The pharmacology of the placenta is very simple. Comparison of the results obtained by the various authors shows that the simplest methods of administration are the best, and that the pulverized, dry placenta taken by the mouth is entirely inocuous. The dry powder produces the physiological effects of the hormone more surely than the extracts of placenta. A combination of synergizing glands would probably be the most effective therapeutic agent in improving lactation.

Antiscorbutics*



EVER since Holst and Fröhlich asserted, in 1912, that the antiscorbutic property of certain fresh vegetables and fruits may be to a large extent lost when they are subjected to a high temperature or are dried, students of nutrition have been more alert to the possible effects of culinary processes on some of the less understood properties of foods. Although, as has already been discussed in these columns, McCollum and his colleagues have assumed that scurvy is a disease related to intestinal putrefaction and the retention of feces, the concordant opinion of other recent investigators, notably Givens, Hart, Hess, Mendel, Steenbock and their co-workers in this country, and Chick, Harden and their collaborators in England, has substantiated the earlier view that the disease is the result of a deficiency of some nutritive factor in the diet. From this standpoint we may speak of the lack of an antiscorbutic vitamin, just as the lack of an antineuritic vitamin is postulated in the genesis of polyneuritis.

The lack of knowledge of the distribution of antiscorbutic vitamins has been accentuated by the needs of infant feeding. The use of cow's milk pasteurized at a temperature as low as 63 C. (145.4 F.) for thirty minutes has led in the course of several months to mild outbreaks of infantile scurvy, thus indicating the poverty of heated milks in the antiscorbutic vitamin. Only recently Hart, Steenbock and Smith have demonstrated at the University of Wisconsin that milk sterilized at 120 C. for ten minutes, commercial unsweetened condensed milk, and the commercial milk powder examined had lost their antiscorbutic properties when used in quantities equivalent to an amount of raw milk which would prevent scurvy in guinea-pigs on a diet of rolled oats and dried hay. From such citations it becomes evident why investigators of infant feeding have sought suitable sources of antiscorbutics and why producers of food preparations are concerned with the retention of native antiscorbutic potency so far as this is possible. Recent writers have sanely summarized the situation by saying that either the results with guinea-pigs on experimental survey should not be translated to infantile scurvy, or we should follow the wiser course of using some antiscorbutic in conjunction with the exclusive use in infant feeding of such heated milk products as have been described.

Thanks to the labors of a number of investigators both here and abroad, the pediatrician is no longer limited to the conventional orange juice in his efforts to avert scurvy in infants. Reference has been made in *The Journal* to some of the novelties, such as the raw juice of the swede and the tomato, which are also available for human nutrition. Although the antiscorbutic value of fruit juices was recognized three hundred years ago, Alice Henderson Smith of the Lister Institute in London has upset the traditional faith in lime juice, as the result of her historical studies. It appears that the juice used with good effect in the olden days was in reality obtained from lemons and sweet limes, not from the West Indian sour limes. With the change to the sour limes has come a failure in antiscorbutic-potency that was difficult to understand until it was demonstrated recently by experimental tests on animals that the sour lime of the West Indies (*Citrus medica-acida*) happens to have only one-quarter of the antiscorbutic value of the lemon (*Citrus medica-limonum*). Lemon juice is easily available for the treatment of infantile scorbutus. Harden and Zilva have further demonstrated that after removal of the free citric acid and other acids from lemon juice, the residue also retains its antiscorbutic activity, and in collaboration with Still these investigators have, for the first time, clinically employed with success this antiscorbutic factor separated from the greater part of the inactive components in combination with which it occurs. The vitamin-containing product could be administered in large dosage after the refinement and the exclusion of extraneous substances. In fact, the lemon product was given in concentration at least double — in one case seven times — as strong as the form in which it occurs naturally in the foodstuff (lemon) from which it was obtained. The treatment was thus, so to speak, "intensive," reminding one of the seemingly potent therapeutic procedure of Hess, who introduced orange juice directly into the circulation of scorbutic infants.

There are indications that the potent fruit juices can be suitably preserved for clinical use. This is a matter of no little consequence in conserving products that do not come into the market with uniform frequency and at reasonable prices throughout the year. Harden and Robison have reported from London that the antiscorbutic principle in orange juice is not volatilized when the juice is distilled at 40 C. under reduced pressure. By evaporation of orange juice at 40 C. under reduced pressure, it is possible to obtain a solid residue which possesses in a very high degree the antiscorbutic value of the fresh juice. This value is not appreciably diminished when the substance is kept in a dry atmosphere at room temperature during six months. The prolonged heating to which fruit juices are subjected in the usual processes for the manufacture of jams and jellies renders it unlikely that these would ever possess any considerable antiscorbutic value. Nevertheless, Harden and Robison have found that by the use of the newer extremely rapid commercial processes of concentration without the application of high temperatures, fruit jellies can be prepared (from the apple, for example) which are by no means devoid of antiscorbutic potency, though this is of a different order from that characteristic of the orange and lemon. Surely there can no longer be any excuse for the failure to avert infantile scurvy, even when fresh, unheated milk is not available.

---

* **Editorial,** *Jour. A. M. A.*, July 26, 1919.

The Prognosis of Albuminuria in Pregnancy*

THE appearance of albumin in the early months of pregnancy, its large amount and its persistence during weeks or months following labor, would seem to indicate a particularly serious prognosis, but experience shows that this is not necessarily the case. It is enough to go over certain case histories to be convinced that women who have had much albumin, which did not disappear from the urine for six months after delivery, nevertheless had future pregnancies without albuminuria. Generally speaking, the prognosis is more serious when albumin occurs in multiparæ who have presented nothing abnormal in their former pregnancies, and in them it would seem that the albumin is more the result of a former bad condition of the liver and kidneys, rather than of the action of the pregnancy itself. On the other hand, in primiparæ the hepatic and renal lesions, which may be grave, even fatal, are usually temporary, are produced by an intoxication of gravidism, and do not manifest themselves in future pregnancies with the same intensity because the organism is, so to speak, immune.

The ultimate prognosis of albuminuria in multiparæ would, consequently, appear to be bad, but it is to be remarked that many women — particularly among the working classes — do not always consult the physician early enough for treatment of accidents of autointoxication, so that proper therapeutic measures are not instituted in time. They come to the hospital when a symptom, such as edema of the lower limbs or hemorrhage, occurs. Unquestionably, a number of women when duly warned will submit to medical care in their future pregnancies and thus avoid the return of more or less serious accidents, but there are also many who take no heed of the warning given.

From present statistics it seems fair to conclude that a woman presenting albuminuria in her first pregnancy is not fatally destined to have it in her future gestations, but when a woman has had albumin in the urine with her first pregnancy and this is again present with the second, the pregnancy will rarely go to term if the mother is not medically supervised. The urine should be examined at least once a week in all cases where accidents of autointoxication have occurred during a former pregnancy, and once a month a complete analysis should be made. The obstetrical prognosis of the albuminurias of pregnancy is all the more favorable, the greater the medical care given during gestation, the greater the thoroughness with which both diet and other necessary treatment are carried out.

The Discovery of Thyroxin*

PERSONS who deal with so-called "practical" affairs, and employ the routine agencies and materials of their vocations or professions, are singularly prone to overlook the labor involved in perfecting what they utilize so effectively. In the hands of the physician, for example, a seemingly simple manometer is made to tell the story of blood pressure in a few minutes; or a complex chemical compound is prescribed with the assurance that it will accomplish a definite therapeutic purpose in each case usually without any realization of the scientific efforts preliminary to the final success. Scientific research would receive a more respectful consideration if its necessity for present-day practice were more definitely appreciated. This prelude is the occasion for reference to some details recently published with respect to the discovery by Kendall of the active iodin compound of the thyroid gland. We have already referred in *The Journal* to some features of thyroxin, as the compound has been designated briefly, and its potent physiologic properties. The investigation of the chemical constituents of the thyroid was begun by Kendall in 1910 at the pathologic department of St. Luke's Hospital, New York. Thyroxin was first isolated as a chemical entity in December, 1914. Since then many grams have been prepared at the Mayo Foundation laboratories in Rochester, Minn.; in fact, about 33 gm. have been separated from more than three tons of fresh thyroid material.

---

* Editorial, *Medical Record*, Sept. 6, 1919.

* Editorial, *Jour. A. M. A.*, Sept. 20, 1919.

The structural formula, indicating it to be trihydro-triiodo-oxy-*beta*-indolpropionic acid was determined in the summer of 1917. Osterberg succeeded in synthesizing thyroxin with its 60 per cent of iodin in December, 1917; and the synthesis and formula have since been confirmed by Kendall. Minute doses, represented by a few milligrams of thyroxin, show the characteristic stimulation of metabolism in man that thyroid medication is known to bring about. Kendall believes that the active chemical groups in thyroxin are essential to the production of energy in the body. American science may take pride in the successful outcome of nearly a decade of patient effort in the laboratory directed to the unraveling of the chemical mystery of the potent thyroid. It is a story of persistent trials in the face of many discouraging incidents. The history of thyroxin, in its early chapters now written where all may study it, furnishes an excellent illustration of that "diligent inquiry and laborious, persistent search of truth" which the dictionary designates as research.

Fever and the Water Reserve: A Physicochemical Theory*

In the course of the important studies by Woodyatt and his associates on intermediate carbohydrate metabolism, timed injections of glucose and other substances being given intravenously by means of ingenious motor-driven pumps, it was observed that under certain conditions fever would result. Fever came on when glucose was injected in such quantities that marked glycosuria and diuresis developed, provided that in the meantime, water was withheld until the body lost some weight. Under such conditions chills were noted also. Naturally the thought arose that under these conditions there might not be enough available water left in the body to cool it by evaporation, but of course the possibility that the sugar injections in some way disturbed a nervous heat-regulating center has to be considered. * * *

The results of the new experiments by Woodyatt and his associates, being made under the best controlled conditions so far attainable, make a significant contribution not only to the study of experimental fever but also to the theory of fever in general. It is remarkable to what heights the temperature of the body may be driven by the method used in these experiments; fever of 111 F. is produced readily, and in one case the temperature of a dog in the course of ninety minutes, rose to 125.6 F., the highest animal temperature on record, as the consequence of a timed intravenous injection of glucose solution during which the fluid output exceeded the intake by 616 c.c. (66.2 c.c. per kilogram). The results show further that increased combustion of glucose is not a necessary factor, and that fever can be produced in dogs that have been rendered poikilothermic by severance of the cervical cord; hence this fever is not dependent on a nervous heart-regulating center.

The outstanding fact in these experiments is that single injections of glucose (and certain other substances like salt and lactose) may produce fever when the body is depleted of water. The condition is similar to the inanition fever of the new-born described by McLane and Crandell, and to the salt and sugar fevers of infants, all of which are relieved by water. These fevers consequently may be looked on as "thirst fevers" due to reduction of the amount of water in the body available for evaporation at the normal temperature. The question arises: "Is the fever of the ordinary febrile diseases of the same nature?"

Balcar, Sansum and Woodyatt have discussed the possibility that the fever of typhoid and other febrile diseases may be the result of a lack of free water, available for evaporation, because the colloids of the body are changed by the poisons of the infection, so that they take up and bind more water than in health. They point out that this idea receives support from concentration of the blood and secretions in infectious fevers, the cloudy swelling of the cells, the thirst, and the sudden release of large amounts of water in the urine and sweat when the fever ends by crisis, as in pneumonia. The liters of water given off during a few hours in such a crisis can be accounted for only on the score of water retention during the febrile stage. Whether we shall be able to measure the variations in the amount of free water in the blood that may occur in fevers remains to be determined, but it is not at all unreasonable to expect that a method that might be suitable for clinical use may be devised for this purpose. We know that plenty of water is beneficial in many febrile diseases, but "probably no one has yet daringly pushed the administration of water in fever to the ultimate limits which might be necessary to ascertain whether every fever can be made to disappear entirely if enough water is given."

The results in this direction mentioned by Balcar, Sansum and Woodyatt are, of course, only tentative as yet, and the outcome of the work in progress will be awaited with much interest. For the present, emphasis is placed on the fact that a new, well formulated and well founded theory of fever is advanced, according to which fever may result from the lack in the body of water available for evaporation, and in infectious diseases such lack may be caused by an abnormal increase in the power of the proteins of the body to absorb and bind water. Undoubtedly this physicochemical theory of fever will prove of much value in stimulating experimental work, and it is possible that it may lead to important advances in the treatment of febrile diseases.

---

* **Editorial,** *Jour. A. M. A.*, Aug. 30, 1919.

Articles of Interest

Suprarenal Cortex Therapy

By S. W. Little, M. D., Rochester, N. Y.

I report the following cases for what they are worth. In each case if medication had anything to do with the result then the credit must be given to the Suprarenal Cortex used as that was the only medication which could have had any possible bearing in producing that result.

In no case was the Cortex used aimlessly but as the result of theoretical reasons based upon several years critical study of the ductless glands. These reasons have been set forth in various articles in the Medical Journals during the past five years. (The references will be gladly given to anyone interested but the supply of reprints is entirely exhausted).

The preparation used was a two grain tablet of Suprarenal Cortex made at the writer's request by the G. W. Carnrick Company.

Case 1. — T. F., male, married. Age 28.

Nov. 1917, a spindle-celled sarcoma was removed from rectum. Prompt recurrence. Stools ribbon-shaped.

March, 1918. Second operation. Again prompt recurrence and April 10th the stools were again ribbon-shaped.

Beginning early in April, 1918, from 2 to 8 grains of the Suprarenal Cortex were given daily.

April 18. Stools circular, size of thumb. Patient eats and sleeps well. Weight 138 lbs.

June 3. Stools nearly normal size. Patient says he "Feels fine," and is working 12 hours a day (he is a farmer). Weight 143 lbs.

July 13. Patient continued to improve until two weeks ago when his tablets gave out and he neglected to get a fresh supply. The surgeon who referred the case to the writer reports that the growth is beginning to enlarge again whereas, while taking the tablets, it had steadily shrunk, rapidly at first and more slowly later. Weight 140.

Patient advised to take 8 grains daily and report regularly but he has never done so and is entirely lost sight of.

Case 2. — W. H. C., male, married. Age 57.

Cancer of Prostate. May 21, 1918, operation attempted but abandoned because of extent of growth and involvement of neighboring parts. June 1st. Condition of patient fair. Appetite, bowels, sleep, satisfactory. Weight 135. Best previous weight, 150. Urine escaped at first through abdominal incision; later this was closed and ever since patient has passed urine through urethra though he has no control and wears a urinal. Was given Suprarenal Cortex, grains VIII daily which has been continued to date (July 24, 1919).

June 15, 1918. Weight 137. Surgeon reports growth smaller.

June 29. Weight 140.

July 16. Surgeon reports growth still smaller and softer. Weight 140. Feels "fine." From that time to the present the patient has remained about the same, the growth remaining stationary about as it was a year ago. Patient reports (July, 1919) that he would have nothing to complain of if he did not have to wear his urinal.

Case 3. — Mrs. B. W., married, no children, age 34. This patient had been treated by the writer for nearly a year before. Much to his chagrin, the patient herself forced the correct diagnosis upon him by calling attention to the gradual "brownish discoloration" of her skin. She had and had had for a year all the symptoms of Addison's disease and until she pointed out the discoloration, the writer's best diagnosis had been "some obscure disorder of one or more ductless glands." Various ductless gland preparations had been tried without much effect. In October, 1914, the belated diagnosis was made and at once the patient was given Suprarenal Cortex, eight grains daily. (The writer contends that in this disease the Cortex is at fault and not the medulla at all primarily. This contention, if true, explains the usual failure of adrenalin medication in Addison's disease, adrenalin being a product of medulla and not of cortex).

From that time until the present (July, 1919), the patient has been persistently well except for two attacks of influenza and except when she went too long without the Cortex medication. At times she will go months without medication, and again only a few weeks without Cortex serve to produce again the anæmia, the lassitude, the skin discoloration, the gastric symptoms, the low blood pressure, etc.

Case 4. — Mrs. L. J. W., married, no children age 35. Another case of Addison's disease of rather mild type like the other though, again like the other, undoubtedly Addison's disease. First seen and diagnosed properly January, 1915. Suprarenal Cortex medication as in the previous case, of which it is practically a repetition. Always sooner or later without the Cortex the symptoms returned to be promptly relieved by the resumption of medication. This patient was last seen in December, 1917, almost two years after the diagnosis was made. At that time she had been without her tablets for two months and came for more because she "was getting tired again and the brown spots were coming back." Experience had taught her how to "get well again." Patient left the city soon after and subsequent history is unknown to the writer.

***Case** 5.* —— (See editorial, *Bost. Med. and Surg. Jour.*, Oct. 25, 1917.)
Mrs. C. V. K., married, age 39.
Ulcer of stomach. First came under observation Nov., 1917. Previous to that time for several months has had several "attacks" characterized by pain in epigastrium, sometimes relieved by food and sometimes not; often vomits during an "attack," occasionally blood, no fever at any time. She was given Suprarenal Cortex, 6 grains daily. Within a few days her "attack" was relieved. Since then she has never had any stomach trouble except on three occasions when she ran out of her medicine or stopped taking it because she judged it unnecessary. On each of these occasions the resumption of the Cortex medication promptly relieved her. Her comments now sound like a patent medicine advertisement as she says that she "will never be without this wonderful medicine."

Case 6. — C. H. W., male, single, age 28.
First seen, Nov., 1917. For past two years has had attacks of what he calls indigestion, characterized by pain in epigastrium soon after taking food. At first these attacks were not severe and passed off in a day or two. Later the attacks became gradually more severe and more frequent and were accompanied by nausea though he never vomited. Had gradually lost weight and strength. The present attack had already lasted two weeks and showed no signs of abatement. Diagnosis: Ulcer of stomach.
He was given the Cortex tablets, 8 grains daily. Patient reported that he was relieved in three days. This of course might have been a mere coincidence except for the fact that, like the previous patient, he has had several "attacks" when not taking the tablets, is always promptly relieved by them and has no attacks when using the Cortex tablets.

These cases are typical of others in which Suprarenal Cortex was used alone. There are many other cases in which other ductless gland preparations were used in addition to Suprarenal Cortex but such cases are not included in this report which is intended to concern Suprarenal Cortex medication only. These other cases are mostly cases of faulty development of one kind or another and indicated failure not of one but of several ductless glands in varying degrees.

It is the writer's opinion that in appropriate cases a reliable preparation of Suprarenal Cortex, given by mouth, is effective to a greater or lesser degree in supplying cortex insufficiency. And it is certain that such insufficiency must produce systemic trouble if only for the reason that the cortex of the Suprarenal gland is essential to life.

Groping in Medicine*

By Beverley Robinson, M. D., New York.

PERHAPS, feeling one's way, would be better and more explanatory. At all events, to some it would seem pleasanter to the ears, as showing something like rational trial and research, or evidence from facts, when acquired. Empiricism, so termed, is in this line, and, alas, so is much today that is called experimental science, based upon laboratory research and essentially attached to the history, development, and behavior of microbes—the bugbear of the younger generation of physicians.

The thoughts that arise in my mind are suggested and furthered by the attitude of many of our guides today *in re* influenza and its treatment. Because we have no specific against it, because we cannot as yet stop its advent and wide dissemination, because we cannot cure it indubitably when it occurs, why do much, or anything, in a preventive, or remedial way, until we shall have surely found a vaccine or serum that will do the job and indeed, one or another, upon which all the experts shall be of one mind as to its absolute safety and reliability?

The truth is, from a broad and sane viewpoint, we do know certain things about as well as they will probably be known in the years to come. We know what our forebears for many generations believed advisedly and thoroughly, and much of this is still good and true and should claim our abiding and unalterable faith. Others are now and were *sub judice*, but should at least have our respectful indulgence as to their merits. I claim even now that Huxham's tincture of bark, the formula of which is over one hundred years old, will still cure, or greatly ameliorate, in most instances, not only malarial fever, but also many febrile conditions of uncertain or unknown provenance.

I claim that since my boyhood days I know of no combined remedies that will soothe, quiet, and help beneficially a patient in many acute ills more than the sweet spirit of nitre and the spirit of mindererus. In an acute cold, when the nose is stopped up, when there are chilly and febrile conditions, a mustard footbath and a hot toddy at bedtime, with or without a Dover's powder, will do the trick when the coal tar products of latter years are prejudicial or worthless. And as to vaccines, or serums, they had far better be left wisely alone, at least for the while. After numerous trials of many remedies and treatments, throughout a long series of years, I have concluded that in salicylate of ammonium I have found the best remedy, preventive and curative, of ordinary colds and also of influenza. It will not prevent or cure all cases, and I know of absolutely nothing that will, but it will be, of all remedies, the least objectionable or harmful. Of course, there are personal peculiarities that should always be considered with remedies, as with foods. Just as eggs are poisonous to a few people, so may salicylate of ammonium be. In moderate, frequently repeated doses, I have yet to meet anyone that was affected in an alarming way. I have met some whose stomachs or ears could not tolerate the salt for long. In regard to the precise dose for anyone, I cannot prejudge, and must rely upon feeling one's way. I already know that, for many, five grains of salicylate of ammonium in a capsule at the beginning of a cold and taken every hour, for five, six, or even ten or twelve doses, is none too much. Thus taken, a beginning cold or influenza may be practically aborted, in some instances, in twenty-four hours.

---

* *Med. Record*, Jan. 25, 1919.

Alas, there were instances, and not a few, in our late epidemic of influenza, in which this, like all remedies, failed. But, is not this true in certain cases of every threatening acute disease and of all remedies yet acquired by our profession through all its long ministry to human ailments? The best, the most learned, the wisest practitioner of medicine, must grope, must feel his way, must often make repeated, intelligent trials before he hits upon the real thing. And even this real thing will go back upon him when he least expects it and when previously he was most hopeful, and then something which he had not hitherto tried in what seemingly was a like case, simply does the work admirably; that is, it relieves or cures the suffering one.

A final thought is this: Every man's experience is his own, not another's. All he can do, therefore, is to report truthfully and advisedly his own findings, trusting to the future and to his fellows to mark what is good and useful and to ignore or pass over what does not fill the bill.

Rectitude in one's statements is what we most want, and if it forms the basis for one's convictions, we must trust the latter until multiplied counter evidence cancels them.

The Pathogenesis of Cancer*

By Charles Green Cumston, M. D.,
Geneva, Switzerland.

CANCER is a dyscytogenesis from local hypocytopoiesis and glandular dysentrophia. In other words, it is a malignant neoplasm characterized by the production of atypical cells resulting from a deficiency in the local nutrition and a disturbance in the entrophic secretions.

Gley classifies the glandular secretions into nutritive and morphonogenetic substances, or harmozones, hormones and parhormones. But according to Naamé, there are some which must assure the function of the intimate nutrition of the gland, that is to say a relationship between cytopoiesis and cytolysis which will allow the gland to repair itself and thus retain its identity. These secretions are termed entrophic by Naamé. Each gland is subjected to the influence of its own secretion and of those derived from certain other glands, and he concludes that there are two types of glandular insufficiency, namely, a simple type of deficiency, and the second or more serious — a qualitative or *dysentrophic* type. If we accept Naamé's theory, there should be a double mechanism in the production of cancerous cells, whether cytopoiesis of an organ becomes lessened from an hereditary meiopragia or on account of age, or from the effects of tobacco or syphilis in the cases of cancer of the tongue, etc. To this hypocytopoiesis corresponds an entrophic secretory disturbance — a glandular dysentrophy — from which a perverted metabolism results, atypical cells develop, and a cancer is produced.

In their paper on endocrine tumors, Gosset and Masson declare that on the first examination of the microscopic sections one would think the specimens are endocrine glands in a state of greater or less hyperplasia and not cancer, and that the regularity of the structure of the malignant growth gives it the histological aspects of glandular tissue. In a remarkable study on cancerous organogenesis Letulle gives his opinion that this process admits the conformation of its metastatic superstructures as being derived from the normal cell type, but embryologically differentiated, from which are derived the embolic elements, so that in reality metastases represent the commencement of the development of organs. Leclerc and Masson (*Société de chirurgie*, November 27, 1918) recently communicated the case of a goitre with metastases which had given rise to a costal growth in a rib on the left side and which after removal resulted in the patient's death from metastases in the spine. Histological examination of the costal neoplasm showed that it was an adenoma of the thyroid, intermediary between the fetal and colloid types. This observation has the value of an experiment in favor of the influence of an internal secretion, unquestionably somewhat changed in the present instance, on the generalization of a tumor which was histologically benign, but assuredly beginning the process of malignancy. Masson's opinion, which seems logical, I think, may be accepted He draws attention to the presence of the exceptional number of kario-kinetic figures seen and perceives in this cytological character — in the absence of structural characters — an element of prognosis. Patel is of the opinion that such instances are merely a generalization of benign growths of the thyroid, but this opinion was offered some time ago so that its present value does not hold.

---

* *N. Y. Med. Jour.*, July 12, 1919.

It might seem that these data confirm the supposition that there may be an affiliation between cancer and the internal secretions, although changed, of the endocrine glands. The cancerous isograft does not succeed but the hemograft does, although it is not always positive, so that the hypocytopoictic and dysentrophic predisposition should play its part. Zoological immunity is to be explained by the differences of the inter-glandular secretions peculiar to each kind, while the individual immunity is explained by the absence of glandular dysentrophy. Although a graft between mice has occasionally been successful, this simply denotes a receptivity belonging to a rudimentary glandular dysentrophy which can undergo an easy dysentrophy. In other words, in order that a cancerous graft shall be successful three conditions are necessary: 1, local hypocytopoiesis; 2, glandular dysentrophy; and 3, that the animal used for the graft shall offer the same interglandular reactions, that is to say that it shall belong to the same species.

Taine and Peyron (*Academie des Sciences*, July 29, 1918) reported a case of a carcinoma of the testicle in the rabbit, with a graft and generalization in the second generation. The animal was eight years old. Fragments of his tumor were grafted in the parenchyma of the testicle of six adult rabbits and subcutaneously in four young rabbits, aged two months. A single graft was positive in the adult animals. This would appear to indicate that glandular atrophy and local cytopoiesis were weak in the latter, nevertheless this weakness was not pronounced, because the evolution of the graft was very slow, as the animal was killed only at the end of two years and six months. The age (on account of use and hyperfunction), heredity, and sex played a fundamental part in the production of the cancer.

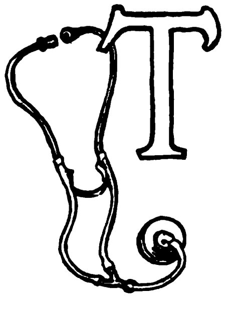
As a subject advances in years, the glands alternate and the cytopoiesis becomes weaker in the organs, and this is frequently according to hereditary predisposition. Women are more prone to cancer, especially of the uterus and breast, given the hyperfunction that these organs are obliged to carry out from menstruation, pregnancy and nursing. Ménétrier's general law, according to which cancer becomes grafted more usually in tissues the seat of inflammation, applies in a remarkable degree to Naamé's conception; in cancer arising in longstanding callous ulcers of the stomach and of the gall-bladder when calculi are present, the gastric and gallbladder hypocytopoiesis must correspond with a glandular dysentrophy, and it is because of an absence of the latter that cancer does not develop in all patients with biliary calculi or gastric ulcer. De Massary has met with the case of a primary cancer of the liver in a young man twenty-five years of age, the histological examination being made by Ménétrier, which showed a cirrhosis of luetic nature. Gilbert, Gougerot, Claude, and Jaboulay have mentioned cancroid degeneration in burns. Jean Minet has reported a case of pancreatic lithiasis upon which cancer developed, and similar cases are common. Even the war has had its quota of cancer, because both Forgue and Bérard refer to traumatism as aggravating, accelerating or even giving rise to cancer, and Beclére declares that a simple wound may be the starting point of a malignant neoplasm.

All this means that there is a precancerous hypocytopoietic state governed by a more or less imminent glandular dysentrophy. The naevi are composed of cells in an incoordinate state, but they represent embryonal débris. Nevertheless they represent cells which are predisposed to ultimate canceration and are not merely predestined to malignant change, as Cohnheim maintained. The very interesting cases reported by Gougerot (*Paris Medical*, August 31, 1919) show that there are late naevi which can be explained by a local dyscytopoiesis. As to buccal leucoplasia, it may be regarded as a precancerous state, and I fancy that this is now generally admitted. As to the very interesting researches of Champy on the evolution of various tissues grown artificially by Carrel's method, this writer found that the cells returned to an indifferent state and cell division occurred in tissues which normally do not multiply. Both are characteristic of malignant growths, but if these tissues are regrafted in an animal the indifferent tissue rapidly retrogresses and proliferation does not take place. This disconcerted state of the cells is due to the fact that in the tissue growing artificially outside the body the glandular secretions are absent, therefore dyscytogenesis, and they exist in the animal receiving the graft, therefore the graft is absorbed. This also explains why Carrel has succeeded in growing cancer cells *in vitro*.

Everything seems to disprove any parasitic or bacterial theory of cancer and much tends to show that opotherapy has a brilliant future in the treatment of malignant disease.

A New Sign for the Early Diagnosis of Incipient Pulmonary Tuberculosis*

By Jorge Vargas S., M. D.



THE new sign which I describe has been found in 169 cases of incipient pulmonary tuberculosis. It consists of the reenforcement of the whispered voice in the vertex of the affected lung. This sign appears before the disease reveals itself by any other symptom, either auscultatory or percussional, before respiratory inversion and impairment in the supraspinal triangle of the affected side, which the classics consider as first signs of the malady, appear. A stethoscope and a little practice are enough to find it. The mechanism of the sign is very simple: it might be said that it is the same as the respiratory inversion, and that, examining not the respiratory noise, but the whispered voice, the physician resorts to a trick which allows him to confirm the beginning of the tuberculous process, in a period before the appearance of the principal respiratory inversion.

**Jour. A. M. A.*, Aug. 30, 1919

It is well known that to auscultation, inspiration is noisy and expiration silent. The murmur is produced, not only by the expanding of the pulmonary vesicles, but because each column of air breaking in the flute-like point which forms each bronchial subdivision has to produce a musical sound. This sound is helped also because the column of air subdivides itself in the thick and narrow tubes. The normal exhaling, however, is silent. Now the respiration of a person at rest, who breathes with the mouth open (as in the position of auscultation) and heard near the mouth, presents a phenomenon quite opposite; the exhaling murmur is produced in the larynx and pharynx, these organs being the first obstacles that the outcoming column of air finds in which it can produce a musical sound. We see, then, that almost all exhaling reenforcement that is found in auscultation is originated in the larynx, the trachea, and the thick bronchial tubes. The ear that auscults hears them, thanks to the fact that they pass through pulmonary tissues more dense which allow sounds to pass better.

Laënnec showed that the first period of tuberculosis is characterized by a peribronchitis; that is to say, an infiltration of the interstitial peribronchial tissues. This sign is a physical phenomenon. The interstitial peribronchial inflammation increases the density of the lung, and owing to the easy transmission of sound by dense tissues, the larynx and tracheo-bronchial noises are transmitted in a better way to the ear that auscults, through a tissue of greater density. This explains the respiratory inversion, that is, the reenforcement of the expiration.

When the peribronchial injury is not sufficiently extensive; when the interstitial tissues of the lung have not yet increased enough to conduct with clearness to the ear that auscultates, the tracheobronchial noise, it is sufficient to make the patient repeat in a low voice in each expiration a word rich in consonants.[1] In an instant the ear will perceive the great difference that exists, in the case of incipient tuberculosis, between the healthy and the affected side. With a stethoscope carefully applied to the ear, isolating outside noises, a very muffled murmur is perceived, at most, from the healthy side, while from the affected side each syllable is distinctly heard, with such force that it reaches sometimes the degree of whispered pectoriloquy.

I have followed the progress of 169 tuberculous patients from the beginning of the malady; in many of them before the appearance of the slightest symptom. Always, sooner or later, this sign appeared before the respiratory reenforcement and other signs that, associated, did not leave doubt for the diagnosis.

Naturally, in cases in which there already exists respiratory inversion, the sign of the reenforcement of the whispered voice is much more accentuated, getting to be, sometimes, almost pectoriloquy. This sign should not be confused with whispered pectoriloquy, which may accompany tuberculous pneumonia of the apex of the lung, which has an acute progress, with blowing and other signs. The cavities are accompanied also by tympany to percussion. The Niess sign, consisting of whispered pectoriloquy in the space situated between the inside edge of the scapula and the columnar vertebræ, is found also in bronchial adenopathy. Its cause is the transmission of the tracheobronchial breath through the hypertrophic lymphatic masses. It has nothing to do, therefore, with that which I have described in this study.

As counter control of the sign of the reenforcement of the whispered voice, I had 140 convalescing and debilitated patients (with uncinariasis, anæmia, chlorosis, etc.) under observation, who did not present the sign.

The sign described appears at the beginning of the tuberculous lung process, when the roentgen rays do not even give a distinct shadow and when there is not yet any other sign either auscultatory or percussional. Moreover, one may easily become accustomed to finding it.

A Safe, Rational Treatment of Neurasthenia*

By Robert H. MacNair, M. D.

WITHIN the past five or six years there have been encountered quite a number of very typical cases of neurasthenia, generally as a result of over mental and nervous strain, with considerable accompanying mind worry. In the very first case encountered, I had myself as a patient, most obstreperously trying subject. Some ancient son of Esculapius contended that "he who treated himself had a fool for a patient" and it was my own experience to fully verify the latter statement. While I continued to remain well enough to keep at work, but suffered horribly from neurasthenic insomnia (which I thought was about the most distressing symptom) I was quite willing to accept almost every suggestion, to try about every new neurasthenic drug that the progressive pharmacists had then put on the market.

Result — I went completely down and out, for the count, as I had to remain in a sanitarium for more than three years. It was in that same institution that I finally found out the inestimable benefit of the drugless treatment in neurasthenia. Hence it was there determined that the course that I had pursued, that I know is still being pursued, in private practice, by a host of physicians, was most decidedly pernicious. Whether or not the course pursued in the said sanitarium was the result of the saving disposition, that the institution would not afford the cost of drugs, it had a very beneficial effect upon my own mind, as it enabled me to distinctly see demonstrated the plain fact that, with absolutely no drugs, the neurasthenic subject would make a surer recovery under favorable conditions otherwise, such as proper quiet, exercise, diet and rest.

---

* *Medical Times*, July, 1919.

And, what is of almost equal importance, there would not be the danger of drug depression (such as hypnotics) or the fixing of a narcotic habit.

The superintendent of that institution repeated the very unfavorable prognosis — that I would never be any better, that I could not hope to recover the normal working power, etc., etc. The fact is, today, just about six years after the said prognosis, I find myself far better fitted for mental work (frequently now, there are eighteen hours out of the twenty-four, with not very long rest periods, spent at work) and there is not one neurasthenic symptom left.

It is quite true that, within a short time after the discharge from the sanitarium, when there was still more or less weakness and uncertainty in the mental and nervous functions, with rather short sleeping periods for each night, I chanced to come across a most useful tablet, of the glandular therapy, it is known as hormotone. As that tablet impressed me as being free from the ordinary drug reaction I readily put it into regular use taking two of the tablets after each meal. Within two weeks after instituting this glandular therapy, I found myself sleeping eight good hours per night and there was a very perceptible, gradual regaining of nerve force.

Within four months of my discharge from the sanitarium I was quite well enough to resume the ordinary occupations of an active life and have kept steadily at it ever since.

While making a professional call at the home of a suburban family, the mother of the home asked if I could spare the time to wait and see her eldest daughter, a most energetic young lady of some twenty-five or six years of age.

The daughter had, during several years, been filling a very trying position at a school, her strength and energy had been decidedly overtaxed and she was then neurasthenic.

It did not require more than ten minutes' conversation with the patient to readily determine that there was very decided nervous exhaustion and irritability. I condemned absolutely the drugs that were then being taken and prescribed as a restorative to the appetite:

Ferri Ct. et Strych.	1 dr.
Ferri Ct. et Quininæ.	2 scruples
Vini Xerici.	4 fl. oz.

Sig. One teaspoonful in water half hour before each meal.

I also gave her carefully planned directions, as to the matter of regular exercise, cold baths each morning (it was then in mid-summer), the careful regulation of the diet and action of the bowels, an acceptable form of diversion each day, etc., etc., but absolutely no form of hypnotic or sedative mixture. At a later period the patient was put upon the tonic treatment of two hormotone tablets three times a day.

By the time that the autumn leaves began to fall the young lady patient exhibited sufficient evidence, both in objective and subjective symptoms, of having quite returned to her normal condition. The patient succeeded in changing her life occupation to more congenial environment and, during the great war period, she was one of the most active, untiring workers at one of the big military cantonments, hence she has remained quite well. I have been most firmly convinced, both in a painful personal experience, and with the experience of patients, that very much harm and little or no benefit is wrought to the neurasthenic patients, along the old line of routine drug treatment.

Duodenal Feeding*

In an account of his experiences of duodenal feeding at U. S. Army General Hospital, No. 41, Buckstein emphasizes the importance of the drop method of feeding, as the syringe proposed by Einhorn may produce distension, pain and nausea. The rate best suited can be determined only by the study of the individual case. Though no definite feeding formula can be laid down, the average mixture employed by Buckstein contained 150 c.cm. of peptonized milk, 70 g. of glucose, two eggs, and 40 g. of butter. In a patient weighing 60 kg., who is at rest, such a mixture given three times a day is sufficient to sustain his bodily requirements. The length of time the tube is allowed to remain must vary with the age and recuperative power of the individual, as well as with the chronicity and severity of the lesion. To determine the effect of treatment the patient is fed by mouth while the tube is still in situ. When the food by mouth can be increased one of the tube feeds is omitted, and finally duodenal alimentation is dispensed with entirely and the tube is removed. On the other hand, if pain recurs on feeding by mouth duodenal alimentation is continued.

---

* *The Lancet.* Nov. 8, 1919.

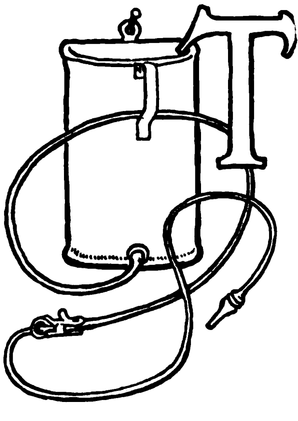
Brief Abstracts

Hypothyroidism in Women — In an able article on ductless gland therapy, J. L. Masterman-Wood (*The Practitioner*, May, 1919), discusses thyroid inefficiency in women and says that the female sex provides the clinician with the majority of cases. At puberty, at each menstrual flow, during pregnancy and lactation, the gland enlarges, which is evidence of the body's demand for further supplies. These constantly alternating periods of augmented functioning and comparative quiescence render the thyroids of women peculiarly unstable.

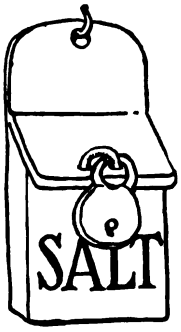
Masterman-Wood points out that thyroid must be administered with discretion in the cases of elderly sub-thyroidics possessing an enfeebled myocardium. He cites an interesting case of a woman of 70 who complained of great weakness, tightness across and distension of upper part of the abdomen, frequent attacks of palpitation and vomiting, extremities always cold. Her digestion was very bad. She had marked constipation, difficulty in breathing, falling hair with baldness of the frontal and occipital regions. The eye-brow sign was marked, the skin dry and harsh and masses of fat had accumulated on the abdomen. There were no heart murmurs but the myocardium was enfeebled and the systolic blood pressure was 170. The urine contained a trace of albumin. In the treatment of this case he ordered her to bed and put her on stomachics and a rigid dietary at first. Later one-fifth of a grain of thyroid extract t. i. d. and Trypsogen with the food were ordered. One month after the beginning of the treatment she was much better in every way, taking ordinary diet. The patient continued taking the thyroid extract in the form of Hormotone Without Post-Pituitary and made a most satisfactory recovery.

Masterman-Wood emphasizes the importance of endeavoring to discover in every case the cause of the thyroid's failure. The exhibition of thyroid extract without the removal of the primary cause will undoubtedly benefit the patient, but remission of the treatment will, in most cases, result in a relapse. Pyorrhoea alveolaris, septic conditions of the nose, tonsils, pharynx, or vagina are causes which must be remedied before a permanent cure can be recorded.

In patients in whom the outstanding features are digestive disturbance and constipation, careful laboratory examination of the feces will place in the hands of the clinician the information necessary for the breaking up of this vicious circle, and thereby pave the way to satisfactory thyroid medication.



The Treatment of Gastric Ulcer by Rectal Injection of Sugar — Dr. George W. Greene, of Auburn, N. Y. (*Medical Record*), says that most physicians give beef tea as a rectal enema, notwithstanding the fact that Dr. Dalton showed a good many years ago that a puppy would die if fed on it, a day sooner than if fed on water. Some physicians give peptonized milk. Dr. Greene has given this treatment a number of times and found that, if the rectum was washed out an hour later, the milk would come away as a curd, not being absorbed at all. If a physician is consulted for ulcer of the stomach, he will give a long list of articles to be eaten. Dr. Greene cannot see how an ulcer of the stomach can be cured while one is feeding the patient, for the digestion fluids will digest the ulcer. He knows from experience however, that they frequently are cured in that way. If one consults a surgeon he will invariably recommend an operation Dr. Greene knows one instance in which a gastroenterostomy apparently resulted in the cure of a bad case of ulcer. For a long time he had treated ulcer of the stomach by sugar enemata. He starved the patient for two weeks and fed him by giving rectal injections of sugar. Three teaspoonfuls of sugar were dissolved in one glass of water, of this solution he gave a syringeful which holds one ounce, every ten or fifteen minutes. He relates one case. Mr. B., a bookkeeper, had had stomach trouble for some time. He would eat a hearty meal, and in about three hours he would have severe pains which could be stopped by eating. There was also tenderness below the ensiform cartilage. He was starved for two weeks, fed with sugar by the rectum. It was remarkable how well he bore the treatment. He did not suffer for food at all. He was first given one-half glass of milk three times a day and the following day was given a whole glass of milk; on the third day he had a glass of milk with one egg beaten in it. The next day he had a full meal. The treatment was perfectly successful, resulting in a permanent cure.



Salt Free Dietary in Epilepsy. —Miralliè (*Bulletin de l'Académie de medicine*, April 1, 1919), allows several kinds of food in the dietary of an epileptic with the proviso that it must be entirely free from salt. He points out that epileptics are often especially fond of this condiment, and the more salt a patient has been eating before the treatment is instituted the better the results are. He says that suppression of salt makes the nerve cells more sensitive to the action of bromide and the dose of this has to be reduced. Patients who have previously been taking from 90 to 120 grains of bromide a day may be reduced to 30 or 45 grains. On a salt free dietary, if the dose of bromide is not reduced, patients show a marked physical and psychic depression. Mirallié gives 15 grains of bromide morning and evening in a tumblerful of water. The results he obtained took place irrespective of the age of the patient or the duration of the disease, and generally the seizures disappeared after the first few days of treatment. He recommends that this salt free dietary be continued at least four or five years, too early cessation often bringing about a return of the seizures.

The patients seem to become thoroughly accustomed to a salt free diet and generally are intolerant of the taste of food containing salt. Later the patient may, if he desires, return to a diet containing salt. Some of them have done so and remained free from seizures for ten or twelve years. Mirallié says that the salt free food constitutes the most essential part of the treatment for the dose of bromide may be gradually diminished or even stopped entirely, hence the patient is kept salt free for a long period.

Of 161 patients treated, 20 were unimproved, 44 showed diminished frequency or intensity of the seizures, while in the remaining 60% the seizures completely disappeared, in some instances for a period dating back twelve years.

Digestibility of Bacon. Blunt and Mallon (*Journal of Biological Chemistry*, May, 1919), questioned the accuracy of Rubner's statement that bacon fat showed a low utilization, 17.4 per cent. of the fat eaten being lost in the feces. These workers' experiments did not confirm this for they found that bacon fat was about as digestible as other soft fat and that nitrogen is also as well digested as that of other meat. The average percentage of digestion of the fat of slightly cooked bacon was 96.3 and of much cooked bacon 97, while the average percentage of utilization was respectively 92.8 and 95.

Hysterectomy in Ovarian Function. Richardson (*Surg. Gynec. and Obstet.*, February, 1919), sums up the evidence for and against the retention of healthy ovaries during hysterectomy. He says that much of the confusion regarding this comes from failure to appreciate the scope and complexity of the problem involved. He claims that it is necessary to have a thorough knowledge of the normal physiology of the ovaries and to inquire from all sources in what respect and to what degree total oblation on the one hand or conservation of ovarian tissue on the other, alters the physiological composite.

He points out that the ovary is a complex glandular organ with a dual function (1) reproduction and (2) the elaboration of one or more specific internal secretions.

The constituents of the ovary are as follows:

A. The ovum possesses a twofold function:

1. Meyer has shown that from the earliest development on to atresia the life of the follicle epithelium depends upon the vitality of the ovum and that if fertilization occurs, the ovum operates to prolong the life of the corpus luteum.
2. The all important function of reproduction of the species.

B. The atresic follicle. This appears to play no part either in menstruation or reproduction. Numerically these follicles constitute the most important epithelial element in the ovary, and our ignorance concerning their function furnishes an argument for ovarian retention.

C. The Corpus luteum. Evidence is apparently conclusive that the cyclical changes in the uterine mucosa are brought about by the specific action of a chemical substance furnished by the corpus luteum.

The ovary governs the growth of the genital tract at puberty, and there is intimate and vital connection of the ovaries with the other units of the endocrine system. He suggests a proper classification of the symptomatology occurring with menstruation and with the physiological as well as the artificial menopause under the following headings.

I. Symptoms from the domain of the autonomous nervous system:
  a. vasomotor
  b. cardiac
  c. gastrointestinal
  d. urinary
  e. endocrine
  f. sweat glands
II. Psycho-neurotic symptom :
  g. psychic
  h. neurotic.

He gives numerous excerpts from the literature on the subject and states that no proper regard has been taken from all the various factors that determine the fate of retained ovaries, without the knowledge of which one cannot estimate to what extent hysterectomy has disturbed their function. These factors are:

1a. A knowledge of the individual patient's condition prior to hysterectomy, both in the psychic domain and in that of the autonomic nervous system.
1b. The cases must be grouped according to age, both at the time of operation and at the time of subsequent observation.
1c. They must be grouped according to the pathology for which the operation was performed.
1d. And with reference to the operative technique, whether or not proper measures were used to safeguard subsequent ovarian circulation.

His conclusions are as follows:

AA. The ovary is a glandular organ of complex function, our knowledge of which is at present far from complete.

BB. The uterus is not essential to a continuation of ovarian function, except as regards menstruation and reproduction.

CC. The advocates of total oblation have not furnished convincing evidence of the correctness of their contention.

DD. The disturbances of ovarian function attributed to hysterectomy are partly those associated with normal menstruation and partly those arising from damage to the ovary through operative trauma or disease.

EE. The weight of evidence furnished by anatomical, experimental and clinical investigations is overwhelmingly in favor of retention of sound ovaries, both before and after the menopause age.

Addison's Disease and the White Line of Sergent. — Mussio Fournier (*Bulletins et mémoires de la Société médicale des hôpitaux de Paris*, March 13, 1919), reports the case of a girl of eighteen who ceased menstruating and showed some loss of weight. A month later she began to experience severe pains in the lumbar regions, radiating to the anterior abdominal surface and even to the thighs. There was also slight headache. By the eighth day the pain was so severe that she went to bed. Next there was vomiting followed by diarrhœa. Upon admission to the hospital the patient was found emaciated and exhausted; temperature normal; tongue dry; pulse rate 120; systolic blood pressure 90; diastolic 60; abdomen retracted and slightly tender, the tenderness being more marked over the lumbar region. Most of the surface of the skin was pale but the parts covered by the corset and garters were decidedly pigmented, as were also the whites of the eyes. The mucous membrane of the mouth showed two small pigmented spots. A distinct white line on the skin appeared in ten or fifteen seconds and lasted three or four minutes. Various tests of the vegetative nervous system gave normal results except that neither injection of adrenalin nor ingestion of glucose brought on glycosuria.

The treatment of the patient consisted in giving forty drops a day of the one in 1,000 adrenalin solution every day. After this the major symptoms disappeared in 24 to 48 hours and the pulse rate dropped from 120 to 80. General vigor returned, the systolic pressure rose to 120 and the diastolic to 90 and the white line phenomenon could no longer be found. However pigmentation persisted and there was still a condition of instability of the pulse — the rate rising to 130 or 140 on exertion, or even spontaneously — and evanescent lumbar pains.

The author confirms the observations made by Sergent as to the value of the white line as an indication of suprarenal insufficiency.

Corpus Luteum in Neurological Practice.—H. Climenko, M. D., New York (*Endocrinology*, Jan.-March, 1919.).

Climenko states that although it has been shown that there is hardly a vital function in the living organism that does not depend upon the internal secretions, and theories have been constructed to explain the relation of psychic processes to variation in secretion of glands, when we come to the therapeutic application of extracts of these glands we are still far from having a scientific basis for our procedure. We are in doubt as to whether extracts of dead animal glands contain the same substances that are produced *in vivo*. The method of action of the organic extract is unknown. The action may be that of the hormone produced in life or it may be the action of dead tissue, *i. e.*, the specific action of new substance.

Climenko gives the results of a number of studies on corpus luteum. Cases in which therapeutic results were obtained as well as those in which they were not, are cited. He illustrates by one case the relation of the pituitary to the sexual glands, and states that amenorrhea should not always be attributed to changes in the sex glands, but inquiry should be made as to the condition of other glands. In one case where the thyroid, pituitary and ovaries were mainly involved, the addition of small doses of thyroid to corpus luteum extract finally cured the patient. Headache that occurs with menstrual disturbance is often relieved by corpus luteum. Climenko found that two grain doses is as large as need be used.

He concludes that (1) corpus luteum extract is effective only in the female; (2) that it acts best when native corpus luteum is present; (3) the administration of the extract cannot replace the function of the native corpus luteum extract in pregnancy and probably also not in menstruation; (4) when menstruation ceases as a result of disturbance of secretion, of another gland, corpus luteum will not produce menstruation; (5) its action is usually prompt; (6) the extract usually gives the same chain of phenomena.

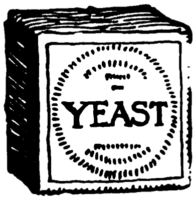
Climenko therefore believes that corpus luteum has a specific action; extracts do not act as the native hormone; the extract in all probability stimulates the native corpus luteum to function. Contra-indications are abnormally low blood pressure and profuse and frequent menstruation.

The Function of the Chromaphil Tissues. — I. Pearlman and Swale Vincent (*Endocrinology*, April-June, 1919).

The authors state that it is not now generally believed that the chromaphil tissues maintain the normal tone of blood vessels or other structures innervated by the sympathetic.

The medulla is not essential to life and large reduction of the adrenin content of the blood does not affect the health of the animal. Rise in blood pressure caused by stimulation of the peripheral end of the splanchnic nerve is not simple, and the curve obtained indicates that more than one factor is at work. The investigations of this curve by numerous observers are at a variance in some particulars and the authors have investigated the subject in experiments upon dogs, cats and rabbits, with ether, morphine, and curare. They find that although the character of the splanchnic curve is greatly modified by elimination of the adrenals, the total rise of blood pressure may not be affected, or may be even greater than before. This indicates that the effect of the adrenin poured into the circulation is to lower blood pressure. In some cases the rise is greater in the intact animal.

The authors find (1) The typical blood pressure curve obtained in response to stimulation of the peripheral end of the cut splanchnic nerve has a sharp rise (having a "hump" about half way up). This is followed by a marked "dip" nearly to the original level, succeeded by a sharp rise. The pressure remains high as long as stimulation is continued. (2) When both adrenal veins are clamped or both splanchnic nerves are cut and the adrenals clamped on the side stimulated, stimulation of the splanchnic gives a simple curve without the "dip." This is not due to damage to the nerves but to interference with the outpouring of adrenin. (3) The dip in the normal curve is due to the discharge of adrenin in such doses as to produce a depressor effect. (4) When splanchnic (peripheral) and sciatic (central) nerves are stimulated in such a way as to give a pressor response, the intact limb follows passively the blood pressure while the denervated limb becomes constricted. (5) After elimination of the adrenal bodies the denervated limb also follows passively the blood pressure. (6) It seems that a discharge of adrenin into the circulation in excess of the usual, would result in constriction in the skin area and a vaso dilation of skeletal and cardiac muscles. (7) It seems probable that chromaphil tissue may influence the distribution of blood, in nervous and muscular strain, if not normally.



The Nutritive Value of Yeast Protein.—Thos. B. Osborne and Lafayette B. Mendel. (*Jour. Biol. Chem.*, June 1919).

The authors note that the war gave renewed interest to the study of yeast as a source of food protein for man. Yeast presents the possibility of a synthetic production of protein from simple compounds, independent of seasons and crops. To determine the value of yeast as a source of protein, feeding experiments were conducted on rats using a diet of dried yeast, salt mixture, starch, butter fat and lard. Yeast furnished the sole source of nitrogen as well as water soluble vitamine. As some of the nitrogen of the yeast is non protein nitrogen, the protein concentration of the diet was probably less than 18%. On this diet rats were kept successfully for more than a year.

Blair Bell on Ovarian Insufficiency

Functional menstrual disorders and menopausal disturbances are usually due to diminished or disturbed function of the glands of internal secretion.

Blair Bell says: "The way seems clear to the solution of the problems which have so long troubled us — the question of a substitution product in ovarian insufficiency. It seems certain that ovarian extract alone is of little value — in spite of a few favorable reports — because after ovarian atrophy or removal, the other endocrinous glands are affected . . . so that ovarian extract alone is not sufficient to combat all metabolic disturbances. If, however, we use our knowledge of the correlated changes in other glands, before long we shall find a combined extract that will give us some measure of success. I believe that the treatment of menopausal disturbances lies in the suitable use of the extracts of endocrinous glands other than the ovary, alone or in conjunction with ovarian extract."

Physicians will find that Hormotone in great measure fills the requirements outlined by this author. Confirmation is afforded by this letter from a physician in London.

"My wife has certainly derived great benefit from Hormotone. She is entering her change of life period after rearing ten children. As she got into a depressed physical and mental state I decided it would be worth trying Hormotone as it promised to help her internal secretions. I now believe Hormotone has given this help."

A Chicago woman physician writes: "Accept my sincere thanks for the Hormotone for my daughter. She is getting well and strong and all symptoms of cardiac trouble and menstrual disorders are gradually disappearing."

In some experiments in which yeast was the only source of water soluble vitamine, the animals grew vigorously to adult size but were usually sterile. To determine the cause of this, rats which had grown to adult size on a 30% to 40% yeast diet were mated with vigorous females which had grown up on a normal mixed diet. Two proved to be fertile, two others failed to breed. Since two out of four rats long fed on large quantities of yeast bred, it indicates that infertility on diets in which only a small quantity of yeast supplied the vitamine was not caused by the yeast *per se.* Animals tolerate large quantities of yeast without toxic action and the usual doses recommended in practice seem to be safe.

Case of Mental Imbecility with Absence of the Sella Turcica. Joshua H. Leiner, M. D., N. Y. (*N. Y. Med. Jour.*, Jan. 25, 1919). Improvement by Organotherapy. Leiner's case shows dyspituitarism coupled with predominant mental defectiveness. The patient, a female aged 12, was stupid, did not respond to questions, was not able to dress herself, had cold hands and feet, and was extremely weak. The shafts of the long bones were abnormally elongated; skin dry; axillary and pubic hair scanty; head asymmetrical with bulging in right parietotemporal region; mandibular prognathism. Adrenal involvement indicated by asthenia and low blood pressure. Roentgen examination showed absence of the sella turcica, digital depressions in all the bones of the skull including the parietal and a slight diastasis of the sagital suture. The symptoms show the lack of function of the posterior lobe or perhaps an occlusion of the infundibulum so that the pituitary extract cannot enter the third ventricle and exert its influence. Treatment consisted of the persistent use of the whole pituitary gland; two and one half grains were given three times daily. Although the patient was 12 years old, by the Binet-Simon scale she showed a mentality of about four years. The improvement was striking and progressive. After about three months' treatment she showed a mentality of about seven years.

The Little Signs of Thyroid Disturbance. — Joshua H. Leiner, M. D., New York (*Medical Record*, July 19, 1919).

The author states that the medicine of the future will be concerned with the detection of "little signs" and not the manifestation of full blown symptoms. This will be especially true in endocrinology. The internal secretion of the thyroid gland affects the organism as a whole and the "little signs" of thyroid disturbance should be looked for. He does not consider in this paper the cases of pronounced hyperthyroidism, myxedema, cachexia strumipriva, etc.

The "little signs" are illustrated in a case of a child six years old. In this case they were sudden loss of appetite, asthenia, constipation with flatulence, drowsiness, subnormal temperature, and slow pulse. Persistent constipation in infancy and childhood and a subnormal temperature and slow pulse are evidence of hypofunction of the thyroid. The thyroid is synergistic to the adrenals and in thyroid hypofunction the adrenal secretion is diminished leading to hypofunction of the sympathetic and consequent muscular weakness.

A case of spontaneous adult hypothyroidism is cited. In this case there were for years the "little signs" of hypothyroidism. The author states the following are signs of hypothyroidism to be looked for in practice — subnormal temperature, slow pulse, gradual alopecia, nutritional disturbances, history of cold hands or feet, lack of initiative, fatigue and tendency to drowsiness in the day. The detection of "little signs" of hyperthyroidism depends on the keenness of the examiner. A case is cited following influenza in which the signs were rapid pulse, tremor of digits, nervousness, cardiac palpitation and insomnia. Usually in a case there will be found only one or two signs. With these as a basis an attempt must be made at classification. Signs of hypo and hyper function may be seen in the same case. For every case manifesting pronounced thyroid disturbance there are at least a half hundred that show only the little signs, and these are the individuals that are usually not diagnosed.

New Theories in Regard to Diabetes Mellitus and Its Treatment. Giuseppe Vigevani, (*L'Ospedale Maggiere*, vii., ser. iii., Feb. 28, 1919).

The author discusses the elimination of glucose and the functional relation between the kidneys and the endocrine glands. It was noted clinically that in diabetes there were variations in the proportion of glucose in the urine, although the glycemia was unchanged. This is explained by recognizing the action of varying amounts of pancreatic secretion and referring it to disturbances (change in equilibrium) of the permeability of the kidney through the absence, insufficiency or qualitative changes in this internal secretion. A priori, the possibility of the secretion of other organs such as the hypophysis exerting an effect cannot be denied.

Nothing is definitely known as to how this impermeability is induced, whether it is a form of action which prevents the Bowman capsule from allowing the escape of the glucose or whether through excitation of another portion of the renal epithelium there occurs a resorption of the glucose itself. It is considered assured that the kidney itself is incapable of inhibiting glucose. This property is, on the contrary, relative, and is conferred on it by factors external to the kidney. The author asserts that the pancreas has a double function on the glycolytic process; one on the liver, the other on renal permeability.

The pathogenesis of diabetes is not well explained as regards its connection with the kidneys.

If the kidneys possess a certain capacity to inhibit or expel glucose, glycosuria is due to the elimination of glucose that the organism has been unable to utilize. Hyperglycemia depends both on the glucose introduced and on its production in the organism and on the rapidity with which it is utilized and eliminated. The normal saccharogenesis is unknown but by injection of phloridzin a glycosuria as intense as in the gravest case of diabetes may be induced. This is accomplished by simple action on the kidneys. This shows that the capacity to produce a large amount of sugar exists even in a non-diabetic organism.

The formation of sugar in amounts greater than can be utilized therefore, occurs without the introduction of substances which normally are not factors in saccharogenesis. When sugar cannot be oxidized and hence cannot be utilized, it may be produced in excessive amounts through stimulations found to be due to organs in a condition of hunger. In grave diabetes the liver cannot inhibit the sugar present in excess in the form of glycogen and thus cannot prevent the development of hyperglycemia.

Adrenaline increases saccharogenesis and the liberation of sugar from the liver and muscles without interfering with combustion.

Probably the pancreas has an action antagonistic to adrenalin as well as an action on combustion of sugar. The importance of the pancreas and other glands and their reciprocal relationship in diabetes is less clear than in experimental diabetes.

The Functional Correlation of the Hypophysis and the Thyroid. — John A. Larson, (*American Journal of Physiology*, June 1, 1919).

Resemblances in structure between the hypophysis and the thyroid have long been noted. In addition to similarities in function in relation to metabolic processes both play an almost identical role in respect to growth. If there is change in structure and function in one following extirpation of the other there is ground for assuming a normally functional reciprocity between the two. Many clinical reports indicate that hypertrophy of the hypophysis follows thyroid disease or deficiency. A summary of the literature clearly establishes the fact that removal of either the hypophysis or the thyroid gland causes definite changes in structure of the other. In the case of thyroidectomy the consensus of opinion is that the hypophysis undergoes hypertrophy.

Hypertrophy of the hypophysis following thyroidectomy has by many investigators been considered evidence of a vicarious relationship between the two glands. Assuming that the hypertrophy of the hypophysis is physiological, the next question to arise is that of the extent to which the pituitary can function for the thyroid. That the substitution, if it exists, is incomplete may be shown by the myxedematous symptoms and often the death of the animal following thyroidectomy. Since the compensatory effort on the part of the pituitary

Rational Treatment of Influenza

Long before the pathologists had incriminated the endocrine organs in influenza, pluriglandular therapy had demonstrated its efficacy in the treatment of this disease and had markedly displayed its usefulness in overcoming the debility attending convalescence. Although the tendency is to put the *onus* upon failure of the suprarenals in influenza, it must be viewed on broader grounds. Greater stress is now laid on the participation of more than one internal secretion in the development of a morbid process, and it is evident from the results obtained with pluriglandular treatment, as compared with those had from the exhibition of epinephrin in influenza, that the endocrine factor is more of the nature of a pluriglandular syndrome than a deficiency of any one particular gland.

Hormotone, which is now recognized as the pluriglandular preparation *par excellence,* has evoked the favorable comment of many physicians in the treatment of influenza and its sequelæ. A physician writes: "Some time ago I obtained Hormotone made by you, and I have to inform you that I was much gratified with the results attending its use. I used it more particularly in cases of extreme prostration occurring as a sequel to influenza in the recent epidemic of what was known as the Spanish form of this disease. I also took some of it myself for several days and was astonished at the difference it made in my sensations. I was favorably impressed with its capabilities."

This is written in October and prognostications by many competent authorities seem to indicate that influenza will once more be rife and that this winter will be a strenuous one for the doctor.

Hence the physician who is looking for a dependable agent in the prevention and treatment of the extreme prostration of influenza will bear Hormotone in mind to his own and his patient's advantage. — Advertisement.

substance attempting to perform a double function in the absence of the thyroid is insufficient, the administration of hypophyseal extract should prove beneficial. Through the adjuvant action of the added hormone the pituitary might now perform its double task.

The effect of the administration of the anterior lobe of the hypophysis to thyroidectomized rats was studied. Two series were operated and fed fresh liver and anterior lobe of the ox respectively in addition to the normal diet. Two other groups were control animals and fed liver and anterior lobe; the amount of liver administered corresponded to the quantity of hypophysis substance.

An inspection of the experimental data in these, shows that the administration of anterior lobe to thyroidectomized rats has a pronounced beneficial action, improving their general condition, accelerating their growth and prolonging their lives.

This may be accomplished by substitution. The structural analysis of the known autacoids of the two glands reveals a sufficient similarity to suggest this. A removal of either gland causes disturbances in carbohydrate and fat metabolism, as well as in the sexual activities and general growth of the body. Therefore even if no iodine be present after thyroidectomy, in view of the similarities noted, it is reasonable to assume that the pituitary hormone can, in a time of thyroid deficiency, take the place of the latter in the metabolic processes.

The objections to the idea of direct vicarious relationship are twofold: the failure to find iodine in the hypophysis after thyroidectomy and the possibility that the hypertrophy indicates pathological processes. On the other hand there is the possibility that the hypertrophy is physiological and that the iodine might not be a necessary factor. Before a decision for or against the idea of a direct functional reciprocity can be reached, more evidence is needed.

Summary

1. The administration of the anterior lobe of the hypophysis has a very beneficial action upon the maintenance and growth of the thyroidectomized rats. Aside from the ameliorating effect upon the general condition of the animal. the life is definitely prolonged.

2. The beneficial effect might indicate a direct substitution in which the pituitary autacoid takes the place of the thyroid hormone, in a compensatory effort to establish normal metabolism. Or the results obtained might be due to a stimulating effect upon the total metabolic processes. A definite decision can only be obtained by extensive study of the various factors involved.

3. An attempt has been made to summarize the existing evidence for a possible direct substitution and to answer objections to this explanation of the results.

Physicians' Library

Book Reviews

The Thyroid Gland. — Robert McCarrison, M. D., Wm. Wood & Co., New York, 1917. Cloth, 286 pages.

McCarrison's work is a concise, authoritative treatise on the normal and pathologic thyroid gland. The sections on anatomy, histology and physiology are well written and form an excellent groundwork for an understanding of the disease processes affecting it. The section dealing with those factors which determine the departure of the thyroid and parathyroid glands from health is especially well written. Those factors are discussed under the following titles:

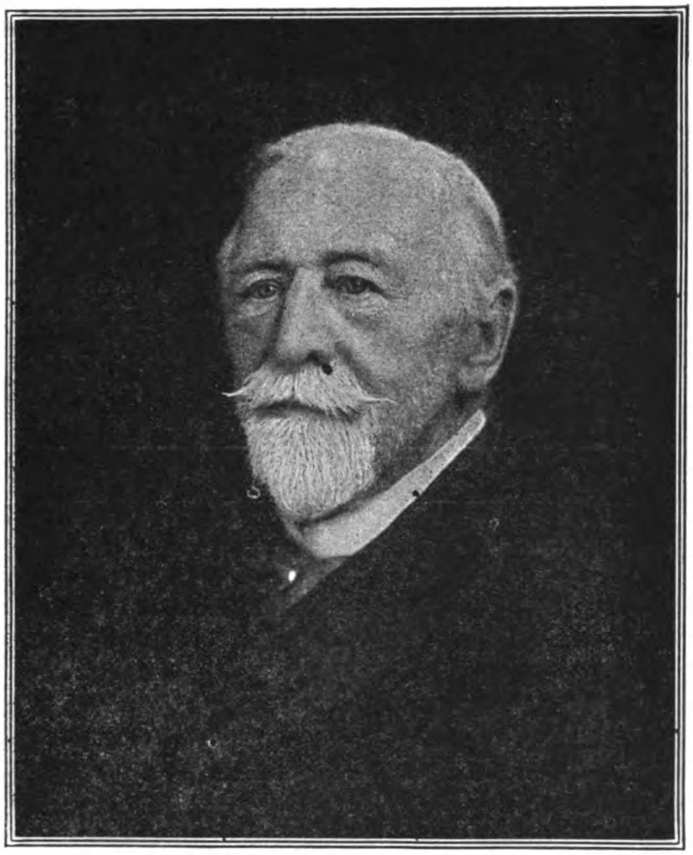
Defective or improper food supply.
Residence in insanitary surroundings.
Bacterial and other toxins.
Infectious diseases.
Constipation.
Intestinal stasis.
Intestinal toxemia.
Fright, grief, worry and mental distress.
Consanguinity and heredity.

The experimental work dealing with the production of goitre by the administration of cultures of fæcal organisms from both goitrous and non-goitrous individuals is original and makes for a clearer conception of the part played by intestinal organisms in causing goitre. When such cultures were administered to rats throughout pregnancy, approximately 63% of the offspring were born with congenital goitre. The chapter on treatment of endemic goitre is helpful and the use of iodine, thymol, naphthol, soured milk, vaccines and thyroid extract is described.

The author reviews the various theories of the cause of goitre and is definitely committed to the theory that the causal agents are micro-organisms inhabiting the alimentary tract of the sufferer from the disease The identity of these organisms is not established but they are presumably anærobic. McCarrison also believes that there is an extraordinary influence of gastrointestinal toxemia in the genesis of Graves' disease.

The diseases of the thyro-parathyroid apparatus are well described: Endemic goitre, congenital goitre, endemic cretinism, tetany, simple toxemic goitre, myxoedema and Graves' disease.

There are 82 illustrations and the photo micrographs are particularly excellent. There is a decided personal tone to the book and a keen analysis of facts is evident throughout. The criticism of much of the work dealing with the function of the parathyroid glands is well taken.



Sir T. CLIFFORD ALBUTT
M. A., M. D., LL. D. and F. R. S.
President of the British Medical Association and one of the grand old men of Medicine.

Sir Clifford, who is in his 84th year, has the distinguished honor of having broken the record in being elected to the Presidency of the Association for four years and will preside at next year's meeting. He has also held the position of Vice-President of the Royal Society.

Known throughout the world as the author of the "System of Medicine," Sir Clifford has been contributing to the literature of medicine since 1871. This exhaustive work is perhaps the most complete in the English language. A genial as well as an accomplished gentleman, his many admirers and well wishers hope that he has many years of usefulness still before him.

The life of Sir Clifford Albutt is an inspiration to the younger generation n medicine.

Our photograph is reproduced by the courtesy of James's Press Agency.

THE DOCTOR

Of all lives the life of the physician is the most self-denying. He has no time that he can call his own. His home is his office, and furnishes him no sweet retreat from irksome care. The night can never assure him unbroken rest. Sundays are often, whether he will or no, his busiest days. He has no holidays, and few and fragmentary vacations. Friendship furnishes him fewer solaces than to other men, for his friends are generally also his patients. He meets men in their morbid conditions—when they are sick and miserable; when they are well he knows them not. He can hardly make a friendly call without the hazard of having it converted, before the evening is over, into a professional one. He fights a battle in which, no matter how many victories he wins, he is sure to be defeated at last—for he is fighting death. And when the defeat, which must come sooner or later, does come, he is fortunate if unreasonable friends do not charge the defeat upon his lack of science or of care. But no man renders a more grateful service; no man comes nearer to our hearts; no man is more beloved. Other services may be as great, but none is more deeply or tenderly appreciated. He summons back from death the child, and puts him in his mother's arms; the wife, and reunites her to her husband. No fee can ever compensate for such a service. He to whom it is rendered is forever debtor to the doctor.—*The Outlook.*

LAUS MEDICI

All hail to the Doctor! The kindliest soul
You can meet on earth's circle from tropic to pole;
A friend ever ready, resourceful and bold,
He is tender to childhood, to young and to old.

From the sweetest of slumbers he starts at your call;
For your rescue and welfare will venture his all;
He halts not to question your rank or your wealth,
But is yours on the moment for succor and health.

Though he seems like an angel in anguish and woe,
His grand self-denial how little ye know!
Ye may search among thousands, yet never will find
Another more truly, unselfishly kind.

And the day is not distant when all shall behold
The Banner of Health o'er the nations unroll'd,
And the Doctor acknowledged, by tongue and by pen,
As the champion of truth and the lover of men!

—R. H. G. Osborne, Morrisville, Pa.,
in *Bucks Co. Med. Monthly.*

.E.C

552

BOSTON MEDICAL
JUN 19 1920
LIBRARY

English Edition 195,000

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

Vol. IV 1920 No. 4

CONTENTS

Pituitary Therapy 75
Organotherapy in Malaria 78
Animal Extracts in Therapeutics 81
Sir William Osler 82
Pluriglandular Theory of the Menopause 83
Endocrinology 83
High Protein Diets and Nephritis 84
Thyroidal Constipation 85
The Pineal Gland, Its Function and Clinical Uses 88
Influence of Pituitary Extracts on the Genital Tract 90
Traumatic Shock and Its Treatment 90
Influence of Thyroid Gland on Formation of Antibodies 92
Gastric Disturbances of Endocrine Origin 93
A Constant Symptom of Hyperthyroidism 94
Glandular Insufficiency in Children's Diseases 94
Book Reviews 97

A Sentinel at the Gate II
The Tuberculosis Case That Hangs Fire III
Secretogen IV
Diabetes Mellitus V
Physician's Price List VI
The Tumultuous Life VII
Hormotone VIII

A PLURIGLANDULAR TONIC OF MERIT

HORMOTONE

INDICATIONS: All conditions dependent on suprarenal insufficiency; neurasthenia; hypotension; lowered virility and sexual neuroses; also menstrual and menopausal disorders.

In neurasthenia associated with high blood pressure and all hypertensive conditions use Hormotone Without Post-Pituitary.

Dose: One or two tablets 3 times daily before meals.

Literature on request.

G. W. CARNRICK CO. 13-15 Laight St., New York City

The Metabolist

A RECORD OF PROGRESS IN THE STUDY OF THE
INTERNAL SECRETIONS AND METABOLISM

Vol. IV 1920 No. 4

Pituitary Therapy

Hidden away in one of the most inaccessible crannies of the skull is a diminutive gland with rare executive ability. A score of years ago it was a mystery, although Galen, long before, thought that he had fully explained its function by showing how it secreted mucus into the nose, whence its name "pituita" meaning mucus.

We are gradually learning that "this queer little morsel of tissue" tucked away under the base of the brain and called the pituitary body or the hypophysis cerebri, is incessantly sending out chemical messengers to all parts of the body to stimulate the processes of growth, the differentiation and replenishment of tissues and to maintain their functional efficiency. These messengers are indispensable for the growth and development of the osseous and sexual systems and together with those of other glands they share in the production of intelligence, thought, initiative and artistic perception. The pituitary is also concerned in the regulation of carbohydrate metabolism, the retention of calcium and other alkalies and the excretion of nitrogen and phosphorus. It is a dominant member of the menstruation chain and largely responsible for the expulsion of the fetus. Perhaps its most extended influence is the maintenance of cardio-vascular tone in conjunction with the suprarenals and much of its therapeutic value is due to this power. This is a good deal to ask of a tiny gland weighing only sixty centigrams, and it is not surprising that it often fails, nor that the complexity of the symptoms of failure should equal the complexity of its function.

Among the signs and symptoms of pituitary insufficiency are mental and physical backwardness, lack of secondary sexual characteristics, cryptorchism, genital atrophy, amenorrhea, impotence, polyuria, enuresis, feminine distribution of hair and fat, dull expression, soft teeth, small nails without crescents, and adiposity. Patients complain of weakness, headache, indifference, inability to concentrate, failure of memory, drowsiness and even somnolence. There may be aberrations of character and temperament, mild psychoses and attacks of epilepsy with vomiting, vertigo, and loss of consciousness.

For oral administration pituitary substance may be given in three forms — total extract, that of the anterior lobe and posterior lobe extract.

Entire Pituitary substance is used in pediatrics, for infantilism, stunted or precocious growth without corresponding mental development, enuresis and hyperplasia of the lymphoid tissues of the naso-pharynx after the removal of adenoids. It is also of distinct benefit in the cases of mentally deficient children of the adenoid type with or without adenoids, and in the psychoses of adolescence. In pseudo-myxedema, rachitis and osteomalacia, it has often been of service. The dose of desiccated entire pituitary substance for children runs from one-half to one and one-half grains two or three times daily.

In general medicine: For exhaustion of the thyroid and suprarenals, especially after acute infections, entire pituitary substance is an invaluable remedy and it is also useful in general depression, inability to work, to think or remember; in the depressive psychoses, threatened dementia praecox, chorea, tetany, paralysis agitans and progressive muscular dystrophy.

According to Pardee one of the first symptoms of a pituitary gland which is functioning improperly is a frontal headache which does not yield to the usual remedies. The patient puts his fingers over the temples to show that the pain "goes right through there." It varies from a dull ache to an intense boring pain. It makes the eyes ache and the head feel as if it would burst. It lasts for a day or two, rather continuously. It may cease suddenly and come back again with exacerbations. Sometimes it comes on with intermittent paroxysms. It is accentuated by excitement, stooping over, and eating sugar. It is often accompanied by nausea and vomiting which gives marked relief. There is usually a good deal of depression. Patients are tired, become stupid, mentally sluggish and very forgetful. They yawn continuously and "want to go to sleep all the time," "feel dopey", have no ambition and do not want to be bothered. In children, there is apt to be evidence of mental retardation with sluggishness of the mind and lack of the higher reasoning powers, while in adults we sometimes see a loss of moral control resulting in frequent visits to the police courts.

Looking at these patients, we notice that the hair is apt to be dark and coarse, to grow very low down over the forehead and at the temples and down the cervical spine. It is abundant over the arms and legs with a curious change in the male to the female type, and in the female to the male. The eyebrows are heavy and long, often meeting in the midline over the nose forming a nasal eyebrow. The female may show a tendency to a moustache. The bones are apt to be either long or broad, depending upon the age when the metabolism was disturbed. The eyes are too close together or too far apart. The jaw is large and the teeth are either widely spaced or are unusually broad. There may be a good deal of adipose tissue. The pulse and blood pressure are both apt to be low, especially during the headache, and the white line of Sergent is very marked, showing suprarenal exhaustion. The sugar tolerance is either too high or too low.

The cause of the headache is hyperemia of the pituitary gland caused by its efforts to meet the demands made upon it from various sources, sometimes an insufficiency in other glands, especially the pineal, the thymus, the adrenals, and the thyroid, while its most common cause is menstruation. On account of this functional strain, the pituitary becomes hyperemic, enlarges and presses upon the walls of the sella turcica with corresponding pain. Whole pituitary gland should be given.

In cardio-vascular disorders when the muscles of the heart and the blood vessels lack tone as in myocarditis, and unstable vasomotor diseases such as the exudative diathesis, urticarias, angioneurotic edemas, rhinorrhea, bronchial asthma, entire pituitary is one of our most valuable remedies. The "Effort Syndrome" or neurovascular asthenia, which is so extraordinarily prevalent and incompatible with working efficiency, is essentially an insufficiency of the pituitary with other coördinate glands so that a pluriglandular preparation should have the preference and, generally speaking, the same may be said of the treatment of all asthenic conditions. The dose of desiccated entire pituitary substance for an adult may run from one to three grains two or three times daily.

Posterior Pituitary Substance should be used in gastro-intestinal atony with bloating after meals, flatulency, anorexia and constipation; in peritonitis and the tympany and hemorrhages of typhoid. In intestinal paresis it affords an additional means of emptying the bowel which is peculiarly applicable and transcends in efficiency any other form of medication.

In acute infections when the blood pressure is falling, the pulse and respiration increasing in frequency, the urine becoming scanty and the strength failing, posterior pituitary substance given hypodermatically is our chief reliance. In polyuria, pollakuria, diabetes insipidus, it is of great service, and in enuresis, its effect is often magical.

Posterior Pituitary Substance is also indicated in disorders of metabolism, associated with increased sugar tolerance and a lack of sugar in the blood, such as myasthenia gravis, hypotonia of muscles and ligaments and the joints; in adiposis dolorosa, dystrophia adiposo-genitalis, and the obesity associated with feminism in the male; in the excessive retention of uric acid in rheumatic arthritis; in inability to retain calcium salts as in osteomalacia and rachitis.

In surgery it is useful to tone up the cardiovascular system before operations and aid in the prevention of shock and collapse, while the treatment of surgical shock has in posterior pituitary substance one of its immediate necessities. The dose of desiccated posterior pituitary substance for an adult runs from one-twentieth grain to one-half grain two or three times daily.

Pituitary Therapy in Gynecology: A profound lack of pituitary secretion before puberty may cause hypoplasia of the uterus and ovaries with corresponding inability to properly menstruate. The girl may feel the efforts to menstruate more keenly than if the flow appeared, although she may be unconscious of the attempts even if menstruation is delayed for years or never appears. When menstruation appears, it is scanty, infrequent, and irregular. If the pituitary function becomes insufficient after the normal establishment of menstruation, the same effects occur. Pituitary insufficiency may result from acute infections, syphilis, tuberculosis or other unfavorable conditions at any time of life and the lessening of menstruation may be a valuable indication of this danger. Many cases of psychoses, acromegaly, dystrophia adiposo-genitalis and other metabolic disorders may be presaged by amenorrhea.

In relative pituitary insufficiency due to hyperovarism, menstruation is too early, too frequent and too profuse. Endeavoring to antagonize this ovarian activity, the pituitary is overstrained, becomes hyperemic, presses upon the narrow walls of the sella turcica and causes violent headache, the most typical and common headache of menstruation. Supplying the lack of pituitary secretion corrects the trouble.

Many a woman's working efficiency is greatly reduced by the cessation of menstruation and the preliminary stages are sometimes more trying than the after effects. For a year or more, there may be marked asthenia, anorexia, loss of weight, and a tendency towards fainting, especially after eating, which is often associated with blurring or even loss of vision. The patient may have severe neuralgia, hysteria or neurasthenia and psychically is often afflicted. She may be possessed of various phobias, mental aberrations, hallucinations, visions and temporary or permanent insanity. These cases are generally attended with low blood pressure and are greatly benefited by the administration of the whole gland. After the menopause there may be sickening sensations of heat (hot flashes), pressure in the head and sweating, dizziness and vertigo. The constant feeling of fatigue is not relieved by rest or sleep, the will power is reduced with a corresponding loss of ambition and interest and there is often pronounced gain in weight. Such cases are benefited by entire pituitary substance but are more often restored to health by pluriglandular therapy comprising extracts of the glands concerned in the phenomenon of menstruation. In such preparations, however, the pressor substances contained in the posterior lobe should be left out when there is a tendency to high blood pressure.

Obstetrics. For the expulsion of the fetus the sensitization of the muscles of the uterus is necessary, and when labor goes over time it is because this sensitization is not accomplished by the pituitary. In this case the whole gland should be given daily in sufficiently large doses to make the uterus responsive to light massage, which may take two or three days to obtain.

In the first stage of labor, when the muscles are inert, in order to bring the head down into the pelvis, posterior pituitary may be given with care and in very small doses (¼ c. c.) repeated as often as necessary. As soon as the muscles become active, it should be discontinued. Anæsthetics and forceps should always be ready. In the second stage, the use of posterior pituitary with anæsthetics gives a quick, easy and painless delivery. The action of pituitary is not hindered by opium, scopolamin or anæsthetics.

In placenta prævia, even when central, posterior pituitary hastens the separation of the placenta, checks bleeding and may diminish the amount of mechanical aid needed. Post partum hemorrhages not requiring sutures are well controlled by posterior pituitary as indeed uterine hemorrhages of all kinds are.

The asthenia of the puerperium may be due to the glands of internal secretion being exhausted in combating the influence of the placenta, and the use of a good pluriglandular tonic embodying pituitary saves the patient much time and distress.

In threatened mammary abscess when the ducts are blocked, the use of posterior pituitary will stimulate the muscles in the walls of the lacteals, squeeze onwards the accumulated secretions, drain the gland and promote absorption without loss of tissue.

In obstetrics, while the posterior lobe is chiefly used for its power to sensitize the uterus and contract its vessels, in cases of high blood pressure it is better to use an extract of the whole gland.

Contraindications for Pituitary Therapy: Pituitary should not be given when there is a history of hyperpituitarism, eclampsia or epilepsy, except where the epilepsy is distinctly due to pituitary insufficiency; when the blood pressure is high, in arterio-sclerosis, nephritis, cardiac complications of goitre, non-compensated heart. Sajous says it should not be used in aortic affections or where there is a tendency to anginal pains which it tends greatly to aggravate. . It is also contraindicated where there is any mechanical obstruction to delivery and, in some cases, of malposition amounting to obstruction.

Organotherapy in Malaria

Prior to the world war, malaria was an ever-important question but now, in the words of a French physician, "Malaria is the order of the day." When it is considered that there are annually one million deaths from malaria in India alone, and that it has been recently estimated that Spain shows a mortality from malaria of over 300,000 every year, no one can deny the vast social and economic portent of this disease.

No phase of the study of malaria is of such importance as the relationship of the infection to the glands of internal secretion. These glands are now known to be among the first factors in the defensive mechanism of the organism. This should be more appreciated than it is, and all the more so because, in the words of Sir Patrick Manson, "We do not cure protozoal infections with drugs; we keep them in check until the resisting power of the patient can overcome them."

Quinine in Malaria: Lately there has been a discussion of the value of quinine; not only as a prophylactic but as a treatment for malaria. Bruce-Porter says that it is only now admitted in India that quinine is not a prophylactic and he adds that he contracted malaria in Mesopotamia in 1916, in spite of a daily dose of quinine. G. Waugh Scott has given facts tending to show that quinine prophylaxis is useless. He divided the labor force on a rubber estate into two sections, the first section consisting of tappers, men of superior physique, better paid, and having lighter work, and a second section which consisted of weeders, among whom there was a large proportion of women and children and elderly coolies. These weeders had harder work and longer hours than the tappers. Each tapper got 10 grains of quinine each day. This was continued for the whole year, 1917, and during the same period no prophylactic quinine was issued to the weeding coolies. The cases among the tappers admitted to the hospital every month gave a percentage of 14.3. The percentage of weeders admitted to the hospital during the same period was 13.19. Scott says when it is remembered that the tappers are of superior physique, it must be admitted that all the valuable quinine that was swallowed by this large number of men during a whole year gave no protection whatsoever against malaria.

Waters, writing to the *Indian Medical Gazette*, has pointed out that many people who never take quinine escape malaria entirely or contract it occasionally and mildly. Cases which have been in the habit of taking small doses of quinine do develop malaria, he says, and are then extremely difficult to cure and constantly relapse, possibly because they have developed in them a quinine-resisting parasite. Waters has also shown that these patients are among those who provide most of the malarial cachexia cases.

A trenchant criticism of the prophylactic value of quinine in malaria is uttered by Johnston in the *British Medical Journal*. Replying to the advancement of the theory of those who say that even if quinine given prophylactically does not actually immunize the patient against an attack, yet it modifies the toxic action of the parasite so that only a mild attack is produced, he advances his own experience in the East African campaign. He has never seen so many cases of cerebral malaria, hemoglobinuria (blackwater fever), in all his twenty-eight years experience in the tropics as he saw in East Africa, yet every one who could was taking quinine prophylactically.

As for the therapeutic efficacy of quinine after infection, some doubt is also expressed as to its true value. Gordon Ward says he pleads guilty to calling attention to the fact that there is something more than quinine administration to be thought of, *i. e.*, "improvement of the natural resistance of the body." He says that blind reliance on quinine ought not to constitute the whole therapy of the disease. He makes the bold state-

Digitized by Google Original from HARVARD UNIVERSITY

ment that "if quinine had never been discovered we should probably know a great deal more about malaria than we do today." Treatment should give its proper place to quinine, but should not therefore deny the efficiency of auxiliary modes of treatment. He recognizes that there is some degree of exhaustion of the secretion of the suprarenal glands, and in the recognition of this suprarenal exhaustion he has strong support, for during the last year or two it has come to be recognized that suprarenal insufficiency is a factor in malarial poisoning, and that it accounts for the asthenia, cachexia, and anæmia so often met with in the disease. The digestive disturbances encountered in chronic malaria may be, in part, also attributed to this insufficiency.

Corfield supports Gordon Ward's opinion that the general and indiscriminate administration of quinine is not sound advice. He says that quinine is the stand-by in acute cases given a few hours before or during the attack, and for some time afterwards, but to give this drug for several months on end to chronic anæmic and emaciated non-febrile cases is folly. A man must "know" quinine and understand malaria. In Corfield's opinion, the cessation of rigors does not mean that there has been any cure of malaria. Later symptoms may and probably will develop, and when these later symptoms follow quinine is to be avoided. The administration of a powerful protoplasmic and therefore metabolic poison to a person whose natural bodily resistance has already been lowered by infection is obviously a practice to be condemned. The danger to be fought against is not the failure to give adequate doses of quinine for a sufficiently long period, but the very opposite—the failure to discontinue quinine in cases showing a post-malarial condition. For such conditions Corfield recommends, among other things, organotherapy.

To clinch the indictment against quinine, Cowan and Strong (Quarterly *Journal of Medicine*, Oct. 1919) are convinced that most cases of malaria are really suffering from quinine poisoning. The amount of quinine that is administered is often large, the smaller doses are continued for too long a time. In consequence a condition of debility is induced which as its cause continues also persists. Heroic doses of quinine, in their opinion, do not cure chronic cases.

Organotherapy in Malaria: In the opinion of many competent observers, organotherapeutic measures offer many qualities not possessed by quinine in the treatment of malaria. In the treatment of the asthenia and anæmia, Benhamou recommends, in addition to quinine, the intravenous use of suprarenalized serum. However, he admits that, in spite of this treatment, the asthenia and pigmentation due to hypoadrenia may persist. He recommends in such cases the exhibition of total suprarenal extract. This would seem sensible and indicates that the suprarenal cortex is also involved; and this is not strange, seeing that the cortex is essential to life while the medullary portion of the gland is not. Previous to Benhamou's observations Paisseau and Lemaire had affirmed that the state of the suprarenals accounted for many features of the clinical picture of malaria, especially in changes in the arterial tension, the asthenia, the lumbar and abdominal pains, the vomiting and diarrhea. The work of these observers has been confirmed by Fraga of Bahia. Suprarenal substance therefore should be one of the constituents of an organotherapeutic product for the treatment of malaria.

There is another phase of suprarenal therapy that demands attention. It has been pointed out that the clinical symptoms of latent malaria are often wanting and that it is necessary to use provocative measures to ensure the presence of the parasite in the blood stream so that it will produce a typical febrile attack and consequently appropriate treatment. Dazzi has experimented with injections of adrenalin and has found that the procedure was always followed by the evidence of the plasmodium in the blood stream, and, in cases in which the parasite was already present, the action of adrenalin caused a striking increase in its numbers while it also occasioned a marked diminution in the size of the spleen. Silvestri has confirmed Dazzi's observations and is of the opinion that the practice of mobilizing the parasite should form an integral part in the actual treatment of malaria, as only by this means is it possible to arrive at complete sterilization of the organism and to treat successfully all forms that have hitherto been rebellious to the most energetic measures.

But further experience has shown us that it is not necessary to employ suprarenal therapy hypodermatically either for the treatment of the asthenia and the low blood pressure or for the purpose of mobilizing the parasite in the blood stream. Suprarenal substance given by mouth accomplishes this end, more slowly, perhaps, but just as emphatically, and moreover, the continuous oral administration of entire suprarenal substance has obvious superiority over the hypodermatic method in its relation to the lasting benefit of the patient.

Spleen Therapy: As the spleen is one of the organs gravely affected in malaria, spleen therapy has been advocated especially where there is definite evidence of enlargement of the organ. E. H. Wright in the *Indian Medical Gazette* has cited two cases in which spleen therapy failed. However, as these cases were acute, they are hardly to be taken as evidence against the usefulness of spleen as this form of therapy has proved its usefulness chiefly in post-malarial conditions. One author has gone so far as to say that it produces the good effects of quinine without its bad effects. Nouveau claims that it is superior to quinine, arsenic or iron in the treatment of paludism. Other authors claim good results, and Paucot of the French Army Medical Corps has used spleen therapy and sums up as follows:

"This treatment has given me results incomparably superior to those which I have secured from other methods of treatment. It seems to be able to succeed in every case of chronic splenitis, save only where the spleen has acquired a stone-like hardness and has become adherent to the diaphragm or abdominal wall. Even then, however, there has been amelioration. The general condition is rapidly benefited. The men are so thoroughly cured that they are able to continue their service, thus obviating a considerable expense and loss of men to the government."

As an instance of the importance that spleen therapy in the treatment of malaria is beginning to assume, may be cited Di Poggio's observations in *Il Morgagni*, June 5, 1919. He says that the only treatment until a few years ago for malarial cachexia consisted in the administration of quinine combined with arsenic and iron. At the present day we have recourse to substances extracted from the animal organism as well. The administration of spleen extract increases the number of red corpuscles and the proportion of hemoglobin. He quotes Maggioni to the effect that spleen extract has the property of a stimulating action on the hemopoietic organs and especially on the bone marrow, which under the stimulation of spleen substance reproduces red corpuscles to make up for those that have been destroyed. Di Poggio himself has given spleen extract in several cases of malarial cachexia with good results.

Pancreas Therapy: Theoretically there is no reason why pancreas substance should not be used also in the treatment of malaria. Improvement of digestion with consequent benefit to the nutrition of the patient would naturally follow from the use of pancreatic ferments. Trypsin and amylopsin have been used hypodermatically by Lamballe (British Army Medical Corps) in the treatment of malaria and he reports good results following their use. He says, "Clinically the results are most marked. The change in the patient within a few hours is remarkable and the benefit permanent."

The thyroid gland with its well-known antitoxic and protective role in maintaining the health of the body would indicate that, in such an infection as malaria, thyroid therapy is indicated. The stimulating effect of small doses of thyroid on the suprarenal glands is well known and this forms additional presumptive evidence of its potential efficacy in the treatment of the profound disturbances induced in the organism by the ravages of the malarial parasite.

Pluriglandular Therapy in the treatment of malaria obviously should be more advantageous than the employment of any one single gland substance. A combination of thyroid, entire suprarenal substance, spleen and pancreas has been tested by a few observers with most encouraging results. While there are not as yet sufficient data to warrant any conclusive verdict, results are certainly stimulating.

A physician writing from Ecuador, says, "All cases of hypertrophy of the spleen due to malaria that I have treated with the combined gland substances have yielded easily and promptly to its use. All of the patients have improved permanently." Another physician in Venezuela writes, "Miss I. O. who arrived here a month ago to recover from malaria had intermittent fever. She could not tolerate quinine, and arsenic gave no results in her case. On the twentieth day after her arrival, I gave her the glandular preparation which was given to me by my friend, Dr.——— On the twenty-fifth day she was cured of the fever and finds herself now, forty days after, perfectly well, and has had no other attack." A London physician states that he has had a number of malaria patients sent to him from the War Pensions Committee, and in those cases where he has used pluriglandular therapy he has found the results better than where he used quinine. "Although the effects of quinine are more immediate and the gland product is slower in action, on the other hand," he says, "the results obtained from using pluriglandular therapy are more definite and permanent."

The following report from a section of Louisiana known to be malarial is of unusual interest. Hazel T———, ten years old, had been treated for malaria with the usual drugs for two years. Her skin was of a dark bronze color, although she is naturally fair. On the twenty-first of September, she was treated by pluriglandular therapy. On the twelfth of October, the patient was many shades lighter in color. Her expression which was formerly fixed became mobile. While she used to avoid other children she became so that she frolicked with them, something she had never done before. On January 6 of the following year, she had grown perceptibly and the skin on the face, ears and hands was clear and fair. She looked bright and cheerful and talked and answered quickly and intelligently. She said she did not feel as sleepy and tired as she used to, in fact, she felt perfectly well. Whereas previously she was constipated, her bowels were now regular, and she had no need to take a laxative.

While these reports from physicians show the great value of pluriglandular therapy in the treatment of malaria, it must be remembered that essentially it is indicated as a means of treating the fundamental changes induced in the organism by the malarial parasite. It does not necessarily mean that quinine should not be employed in suitable cases and at the proper time. It simply means that in organotherapy the physician has a valuable addition to his armamentarium in the treatment of the disease. It should also be borne in mind that while quinine may act more quickly in demonstrating its effect in an acute attack, that the effects of pluriglandular therapy are more lasting, and therefore in the end more beneficial, because they tend to the "improvement of the natural resistance of the body."*

---

* The attention of physicians who are interested in the treatment of malaria is invited to the announcement on page 96 of this number of THE METABOLIST. Their co-operation is heartily invited.

Animal Extracts in Therapeutics

Laboratory pharmacology has developed rapidly during the last decade. With improved and ingenious methods and technique, pharmacology has furnished a rational explanation of many therapeutic agents, and has in precise terms defined the mode of action of many drugs of age long use. Not only therapeutics, but experimental physiology as well, owes a debt to this rapidly developed science. With full appreciation of everything attained, however, it is conspicuous that there is frequently a decided lack of consonance between the findings of the pharmacologist and the observations of the clinician. The physician sees marked therapeutic effect in drugs stated to be inert by the pharmacologist; the active principles of botanical drugs fail to give the full therapeutic effect as observed at bedside by preparations of the crude drug; marked and constant reactions to chemical substances in animals fail to occur or are inconstant in man.

The action of animal extracts in most cases still awaits explanation by laboratory methods. There are, however, several notable examples of carefully worked out physiological action. Pituitary extract (posterior) has been carefully investigated. It stimulates active cells — gland and muscle. It produces rise of blood pressure, contraction of vessels and force of the heart beat. It affects the plain muscle of the intestine, bladder and uterus. It increases diuresis by a direct chemical excitation of the renal cells (Schäfer).

On the other hand there have been no active substances isolated from the anterior lobe of the pituitary which will account for the entire physiological function of the organ, and yet all the evidence indicates that substances from the anterior lobe play an all important part in metabolism.

The action of adrenalin, the active substance of the suprarenal medulla, is also well known. Its action is brought about by stimulation of the sympathetic nerve endings. It stimulates the heart and causes rise of blood pressure and there is contraction of the peripheral arteries due to direct action of the active principle upon the contractile tissue. From the adrenal cortex no active principle has been isolated and yet there can be no doubt that it plays an essential part in the organism. Its hypertrophy during pregnancy and its relation to the development of the sexual organs are well known.

These illustrations make it clear that the complete action of animal extracts can not today be described in the exact terms of laboratory experiment. Animal extracts furnish not only hormones which may merely supply the product of a diseased or non-functioning gland but they may supply some intermediate elements needed in metabolism.

It is interesting to note Schäfer's statement as to the function of the adrenal cortex. "There is no evidence that any kind of active autocoid substance is produced by the cortical cells, and it is probable that their function is associated with the building up of metabolic products which are to find employment in other parts of the organism."

The mechanism whereby body cells take from the circulating blood and lymph those hormones and other products of the endocrine glands for which there is an immediate physiologic demand is not fully understood. Such a selective affinity might be explained by some such hypothesis as "Ehrlich's Side Chain Theory." It suggests analogy to the process in which body cells select particular amino acids, the "building stones," from the proteins which are absorbed in the food. In both cases the cell appropriates from a variety of substances only the ones needed for its particular metabolism — all others pass on and are oxidized or find other uses.

Endocrinology owes both its creation and development to the correlation of clinical observation with pathology. Pharmacology and chemistry offer much promise of valuable aid in its further development but it would be a step backward to neglect the use in experimental therapy of those animal extracts which up to the present time have not yielded active principles or definite pharmacologic action. The clinical observations of the mass of physicians may determine the value of a therapeutic agent in larger measure than laboratory findings.

Sir William Osler

The death of Sir William Osler marks the passing of one of the brighest lights in modern medicine. Dr. Osler's career and fame were intimately linked with America.

Dr. Osler was born at Bondhead, Ontario; was educated at Toronto University, and was graduated as a physician from McGill University, Montreal in 1872. He was professor at McGill, the University of Pennsylvania and Johns Hopkins University. Osler was one of the leading figures in the group of brilliant men who made Johns Hopkins Medical School the foremost institution of its kind in America.

Dr. Osler resigned his chair at Johns Hopkins to accept the appointment as Regius Professor of Medicine at Oxford. He made a strong appeal to his associates, and influenced the lives of many of the young men who were privileged to know him. He was a great writer and a great teacher, and perhaps the ablest internist of his time. It has rarely been the privilege of a man to so influence the thoughts of fellow members of his profession, as did William Osler. His contributions to medical knowledge have greatly enriched contemporary literature.

Why Not Idealize the Doctor Some?

"He took the suffering human race;
He read each wound, each weakness clear;
And struck his finger on the place
And said, 'Thou ailest here and here.' "

Matthew Arnold.

IN MEMORIAM

Dr. William B. Fletcher, of Indianapolis

We men idealize the chief of men —
Idealize the humblest citizen —
Idealize the ruler in his chair —
The poor man, or the poorer millionaire;
Idealize the soldier, sailor, or
The simple man of peace—at war with war—
The hero of the sword or fife-and-drum.
Why not idealize the doctor some?

The doctor is by principle, we know,
Opposed to sentiment; he veils all show
Of feeling, and is proudest when he hides
The sympathy which natively abides
Within the stoic precincts of a soul
Which owns strict duty as its first control,
And so must guard the ill, lest worst may come.
Why not idealize the doctor some?

He is the master of emotions, he
Is likewise certain of that mastery —
Or dare he face contagion in its ire,
Or scathing fever in its leaping fire?
He needs must smile upon the ghastly face
That yearns up toward him in that warded place
Where even the saint-like Sister's lips grow dumb.
Why not idealize the doctor some?

He wisely hides his heart from you and me —
He hath grown tearless, of necessity —
He knows the sight is clearer, being blind;
He knows the cruel knife is very kind;
Ofttimes he must be pitiless, for thought
Of the remembered wife or child he sought
To save through kindness that was overcome.
Why not idealize the doctor some?

Bear with him, trustful, in his darkest doubt
Of how the mystery of death comes out;
He knows — he knows — aye, better yet than we,
That out of time must dawn Eternity;
He knows his own compassion — what he would
Give in relief of all ills, if he could,
We wait alike one Master — He will come.
Do we idealize the doctor some?

James Whitcomb Riley,
April 29, 1907. in the *Indianapolis Star.*

The Pluriglandular Theory of the Menopause*

What may be called the pluriglandular theory of the menopause is one of the most brilliant and also most practical contributions to our knowledge of the functions of the ductless glands and since it confers a far better understanding of the two most important epochs in the development of the individual from birth to death than we previously possessed, it seems very desirable to interest the medical profession in the study of the relationship of this theory to the formation of these periods both when they occur normally and abnormally, which, unfortunately, is only too often the case. for perfect health is a rather Utopian ideal.

One of the essential functions of the endocrine system (in close collaboration always with the nervous system of the vegetative life) is, precisely, to preside over the morphological development of the organism. At present we can determine with sufficient exactitude the effect of the various organs of internal secretion in the evolutionary process; and we know that the great critical periods of this process — the transition from infancy to childhood; puberty; the separate phases of sexual life, especially pre-eminent in women; the climacteric change, and the senile decline of the vital curve — correspond to the occurrence of intense reaction in the glands of internal secretion, which we have called "endocrine crises." Of these, the most interesting revolve around the sexual factors, as does everything in life; these are puberty and the menopause, the rising and the setting of genital activity, between which points is comprised the fulness of human life. In our other book, some years ago, we set forth the general lines of the endecrine theory of these divers periods of vegetative evolution; without preventing our going more fully into others later on, in this book we will deal exhaustively with the menopause, which is the most suggestive for the psychologist and the physician.

One of the fundamental ideas which has been evolved by the intense study of the internal secretions during the last few years, and which is now generally accepted, is the belief that the glands do not act independently of each other but that each is dependent upon the functioning of others for the perfect performance of its specific task. There is a close correlation of functions so that if one gland fails in any way the others react very quickly and endeavor to compensate the disturbances caused by the delinquent gland. This intimate and prompt correlation of the ductless glands is conspicuously manifested in the physiologic transition periods such as puberty, pregnancy, etc., and we are justified in inferring that this same correlation presides over the establishing of the menopause. It is somewhat surprising that this important inference has not been practically applied by the writers who have been studying the critical age and especially so because it only needs a rapid review of the subject to enable one to see the readiness with which the usual phenomena of the menopause find their pathogenic explanation in our knowledge of the endocrine glands.

What causes the endocrine crisis of the menopause? What glands are chiefly concerned in its production? In our opinion, there are three fundamental ones: the glands of reproduction, the thyroid and the suprarenals. These three have a constant action on the somatic and the functional changes which characterize the menopause, and the hypophysis, according to my view, has only a secondary although probably, equally constant influence.

Endocrinology*

New chapters are being written in medicine, and one of the most important of these is endocrinology. Gross anatomical and physiological changes due to the removal or malfunctioning of various glands of internal secretion have been observed for hundreds of years. The high pitched voice, skeletal changes, and various feminine characteristics are well known in eunuchs. In Graves's disease we find tachycardia, rapid speech, exophthalmos, perspiration, loss of weight, and other well marked physical and psychical changes. And so, little by little, we have come to recognize the grosser changes due to disturbance in the endocrine glands. The laboratory has also contributed its findings on the subject of endocrinology — substances affecting blood pressure, striped and unstriped muscle fibres, the oxygen linking qualities of the blood, calcium metabolism and many other vital functions have been attributed to one or another of the glands.

The subject of endocrinology now has a new impetus and is being attacked from a new angle. It is felt that this new method of attack, the clinical, will prove of greater value than former methods. More detailed observations have been made and various endocrine types have been noted. Minute landmarks — the arrangement and texture of the teeth, the distribution of the hair, the coloring, the location of various forms of pigmented moles, the position, shape and size of the ears, skeletal proportions — these and many other markings have proved of service to the careful worker in endocrinology. It has been shown that certain types dominated by one or another of the endocrine systems are more susceptible to certain diseases and are more likely to be unfavorably influenced by certain drugs.

Another important point emphasized by modern workers in endocrinology is the correlation of the various glands of internal secretion, which at times assume each other's function either wholly or in part. Again, a gland may appear to be at

---

* From *"La Edad Critica"* (*The Critical Age*), by G. Marañon, Madrid, 1919.

* *New York Medical Journal*, Feb. 7, 1920.

Digitized by Google Original from HARVARD UNIVERSITY

fault and the entire organism may be suffering from the effects of excessive secretion discharged into the circulation, when the fault lies in another gland, remotely situated, whose secretion or lack of secretion is causing the hyperactivity of the gland under suspicion. The surgeon will often attack the innocent gland and not be able to account for the failure of the operation.

Formerly the dose of a given endocrine gland was based on the gross changes it produced; this was due to the radical requirements of myxedema and other well marked abnormalities. Recent findings, however, have demonstrated that an extremely minute dose often suffices. Sterility has frequently been overcome by minute doses of ovarian gland. Sometimes the difficulty has been attributed to a lack of stimulation of the gonadal glands from the adrenals or the pituitary, and the ovarian difficulty has been overcome by small doses of these glands. Headache caused by hypersecretion of the pituitary, due to a failure of the check exerted by other glands, has been overcome by feeding adrenal gland in small doses. On the other hand, headache may be caused by a hypersecretion of the adrenals causing an adrenal drive, and this in turn may be remedied by glandular therapy which will tend to overcome this tendency.

The chief immediate benefits will be derived in the realm of diagnosis. Landmarks, such as dental formation due to gonadal abnormalities and changes in tooth structure caused by the faulty metabolism occasioned in various thyroidal states, often prove of great value, enabling the observing clinician to use these as indicators of the more important underlying changes.

* * * * * *

High Protein Diets and Nephritis[*]

The science of pathology is still far from formulating an entirely satisfactory hypothesis for the genesis of all forms of nephritis. It is known, of course, that incident to the attempts of the kidney to eliminate certain substances like the salts of mercury or uranium or several other metals, a tubular nephritis of varying intensity may arise; and the acute injury may subsequently become chronic in its manifestations. There is considerable justification for the belief that the reaction of the secreted urine, which in turn is dependent on the nature of the food intake, is not without influence on the behavior of the kidney cells under secretory stress. Usually, however, the etiology of nephritic changes is sought in some foreign factor, such as the inorganic possibilities just cited, or nephrotoxins or nephrolysins assumed to arise within the organism itself.

Although the alleged "strain" of eliminating a large quantity of those substances, namely, the products of protein catabolism in the body which the kidney is normally intended to excrete, has been pointed to from time to time as a possible cause of kidney damage, there has been little convincing evidence for such an outcome. Urea, which represents the great bulk of the nitrogenous waste, is evidently excreted with great ease. There are numerous recorded instances of large increments in urea output without any signs of kidney defect or detriment; but experiments to determine the functional efficiency of the kidney have usually been of comparatively short duration. The clinical forms of nephritis are frequently slow in making their appearance. Newburgh has therefore attempted, in the department of internal medicine at the University of Michigan, to ascertain whether nephritis will be produced when the kidneys have been eliminating an unusually large amount of nitrogenous material over a considerable period of time. He argues that just as the kidney secretes ordinary medicinal doses of mercury without harm, but is injured when the quantity offered for elimination in a given time is augmented greatly, as it is in acute poisoning, so the renal cells may react unfavorably if the quantity of some or all of the nitrogenous substances secreted is increased and kept at the higher level for some time. In feeding experiments on rabbits, renal injury was quickly and constantly noted in animals that ate several egg whites daily. Prolonged egg white feeding caused acute and subacute nephritis. When the nitrogenous metabolism was increased by means of casein, rabbits suffered no demonstrable renal injury from eating 15 gm. of casein daily; but when the daily intake of casein was 30 gm. and the nitrogen metabolism was about three times normal, a well marked deleterious effect on the kidney was produced. Rabbits that lived for months on soy beans, which are rich in vegetable proteins, regularly acquired chronic nephritis and frequently died of it. The nitrogen metabolism from this diet was about twice the normal.

We may accept these observations, which are likely to be widely quoted by the advocates of a low protein diet or at least of greater economy in the use of protein, without admitting their wider significance in the etiology of human nephritis. The vegetarians will find little solace in the fact that sources of plant proteins were involved as well as the tabued animal products. Urea *per se* is not charged with the harm done. It must be remembered that the diets used by Newburgh were potentially acid in character, and certain to produce an acid urine in a species adjusted and accustomed to secrete an alkaline fluid under a free choice of food. Until such experiments are successfully duplicated under conditions in which the normal reaction of the renal secretion is not tremendously altered and the accessory factors in the diet are known to be adequate, the incrimination of the high protein diets in connection with nephritis must be considered with judicial reserve.

---

[*] *Jour. A. M. A.*, Jan. 19, 1920.

ARTICLES OF INTEREST

Thyroidal Constipation*

BY SPENCER G. STRAUSS, A. B., M. D., NEW YORK.

Before venturing into a comparatively new therapeutic endeavor it is wise to glance back over our accepted classical conceptions through whose deficiencies we have come to feel the need for progress. No advance could have been made in the science and art of medicine if we had not been willing to face our own shortcomings squarely. Let us agree that we are becoming more and more willing to regard states of pathology, *i. e.*, diseases, and their therapeutic correction as individual problems in contrast to our former rather indolent mental habit of thinking of the medical correction as fixed by rules, once the pathological diagnosis is established. Anatomy is not fixed and permanent, nor is physiology, nor environment, nor heredity, nor pathology. By the latter I mean states of illness. Surely every human being differs from his fellows externally and so more surely differs in the forces that have gone to cause apparent differences. It should be our attempt to find how individuals differ so widely, and in that answer lies the answer to the question of the variation in disease states, and therefore, to the variations in the correction of those states.

We have learned to regard constipation as a condition of delayed evacuation of intestinal food residues frequently associated with a quantitative deficiency and a qualitative alteration of the fecal mass whether this is purely functional in origin or dependent on organic disease. This is true as far as it goes, but it does not go far enough. Why are some individuals so troubled and others not? To fully cover the causes of constipation we must read through numbers of great volumes and in the end find that a few essential features stand emphasized. Efficient intestinal peristalsis depends on the strength of the bowel muscle, the tonus of the nervous mechanism, and the quantity and quality of the intestinal contents. Any great alteration of these factors from the normal may cause constipation.

A further subdivision is usually made depending on whether the cause be organic or functional. Among the former we find partial lumen obstruction due to adhesions or bands involving certain intestinal segments. Similarly abdominal or pelvic organ displacements, or tumors, may cause such a condition by pressure from outside of the gut lumen. We find organic changes in the gut itself both of congenital and acquired origin, chief among which are the various degrees of ptosis and dilatation. Beyond this, any organic change in the extra intestinal part of the mechanism of fecal expulsion may be responsible. Among these the most frequent is probably perineal laceration in the female. Bearing in mind that we usually divide the functional type of constipation into the subclasses atonic and hypertonic, we include the following as the important causes of constipation of these types. In the first place, psychic causes which result in intestinal atony. We are told that individual habit holds a prominent place among these. So do we frequently admonish our patients to foster the habit of regular and continuous attempts at proper bowel evacuation. Diseased conditions of the upper alimentary tract, notably the stomach, may so affect the intestines that either a condition of atony or spasm results. Particularly does hyperacidity have a constipating effect.

Qualitative and quantitative factors in our food intake certainly affect the expulsive function of the intestinal tract. Probably each gastroenterologist has his own pet dietetic schemes and ideas. Changes in the intestinal flora exert a positive influence on their function as do local areas of inflammation. And finally we are taught that too sedentary a life and improper modes of dress may be the sole fault. So we have indeed a large variety of causes to choose from and can surely satisfy our patients, if not ourselves, when they ask the invariable "Why?" And when we agree with them that this fault must be corrected and they ask us "how", what an enormous variety of therapeutic methods are presented to us for our choice. In the first place, dietetic regulation alone is sufficient in some cases to affect an apparent cure. While on the other hand, the majority require a further remedial measure, be it mechanical, electrical, hygienic or medicinal. The former three are too uncertain in their effect and insecure in their protean characteristics to warrant description here.

Among the most important drugs used in this connection are aloes, cascara sagrada, magnesia, phenolphthalein, podophyllum, rhubarb and senna. The salines are used for a positive temporary effect, the important ones being magnesium and sodium sulphate, potassium and sodium tartrate and sodium phosphate. More recently agents which act mechanically in the intestines have been introduced. The mineral oils for simple lubrication and substances which bring about bowel evacuation through the formation of a large intestinal residue such as bran and agar-agar. There is no doubt that there is a strong feeling away from drugs for overcoming this condition, for we realize, as does the public, more and more, that the cathartic habit is one of the easiest formed and one of those broken with the greatest difficulty. As a matter of fact, most patients have tried one or more laxative or cathartic remedies for various periods of time before asking our aid and the clever clinician usually makes the valiant attempt to remove the remedial drug which the patient has discovered for himself. The thought appeals to the patient. But unfortunately, the doctor's effort is rewarded with little success and he may be forced to prescribe a rarer drug, which the patient has never seen advertised, and this poor layman, being ignorant on the subject, goes his way believing that everything possible has been done for him.

So we have open to us, in our attempt to correct our patient's difficulty, a wide variety of paths, Our efforts will often undoubtedly be rewarded with success, if not complete, then surely partial. But only too often does the patient return, our therapeutic measures having been withdrawn after a conscientious trial, complaining that the old state of affairs has returned. And why this ultimate difficulty? It is because we have devoted our energies to defining a local condition and applying a remedy limited in its effect to the correction of this pathological detail. A local remedy for a local symptom. How narrow.

The day has come when we must regard the individual and his physiology, whether it is normal or abnormal, as a unit. We must ask ourselves why does the intestinal tract of this individual refuse to do its share, but at the same time, recognizing clearly that a big constitutional reason underlies that local manifestation of inadequacy. We must recognize that the only hope of cure for this local error is a deeper correction and we have the means at hand. Let us forget our patient's bowels and his defecatory difficulties, and let us look into the biological soul of the patient himself. Let us try to see in a bigger way how this individual differs from others physically. Let us analyze him from the endocrinological viewpoint.

The glands of internal secretion are gaining a position of growing importance in our medical knowledge and what a few years ago was so keenly interesting by its novelty, is today accepted as common knowledge. Today, those clinical pictures due to disturbance of the endocrine chain which are universally accepted, are the full blown, complete syndromes, such as gigantism, cretinism and the like. But let us pause for a moment. Prophylaxis is the watchword of modern medical and surgical science. There was a time when surgery was a rare and risky therapeutic means. Does the surgeon today wait until pus has broken into the peritoneal cavity before he advises and undertakes the appendectomy? Does the clinician wait until his patient's entire family has contracted scarlet fever before isolating the original focus?

We recognize without a doubt the value of looking beyond the immediate phenomena in our richly rewarded effort at prevention. So, flushed with the successes due to this mode of thought, let us not grow myopic when we travel into newer fields. The signs and symptoms of thyroid deficiency are so numerous, so varied, and yet frequently so slight, that we often in our ignorance or stubbornness, and more frequently in our haste, fail to give the aid we could to such patients.

We must look for both subjective and objective symptoms in our patients which interpreted in the light of our knowledge of the endocrine glands and their physiology, denote slight derangements and alterations from the normal which can be successfully corrected by medical means: whereas, if such deviations were allowed to increase, we would be faced with a complete picture of endocrine pathology, of a surety easy to recognize, but unfortunately, no longer in a state where our therapy would avail.

Throughout the literature we find references to thyroid therapy for the cure of various states of constipation, but apparently this path has been advised and followed in a purely empirical way with the resulting disastrous effect that the busy practitioner is now likely to use this latest addition to his therapeutic armament as harmfully as he formerly did the common garden variety of cathartic pill. Thyroid extract, however given, is not, nor will it ever be, a constipation remedy: nor can it ever become a cure for constipation as such unless in its administration it corrects a constitutional defect which predisposes the individual to an abnormal metabolic state, which in its manifestations includes a deficient bowel evacuation constipation.

We must have regard for the rest of the picture, however, and only prescribe thyroid extract when we feel justified after a careful physical analysis that we have to deal with a case of thyroidal disbalance. In this connection it is wise to mention that the thyroid gland in the human physiology seems to act, not alone by virtue of its own inherent qualities, but by its peculiar ability to activate and coördinate the functions of the other glands of internal secretion, and in this way we may obtain happy results from thyroid therapy, inasmuch as we have indirectly stimulated a gland other than the thyroid to a greater activity through our efforts while the patient's thyroid gland remains normal. Roughly comparing our endocrine organizations to a cartwheel we could give the thyroid the hub position with its activities radiating through the various spokes each representing another gland of the group. The rim of the wheel representing the final individual gland tone.

Let us try to make our therapy as specific as possible and only employ thyroid extract when the thyroid regulation is essentially to blame. This blame must not be laid definitely upon that member until we have evidence enough, after careful search, to condemn it. Clinical study shows that various qualitative and quantitative physical marks are characteristic of thyroid disbalance *per se*. They cannot be proved as yet in the laboratory, but they are valuable nevertheless.

For sake of convenience I shall briefly indicate the more usual thyroidal marks which when combined with the so-called constipation call for the thyroid therapy, such therapy would then in all probability be specific.

Thyroidal Indications

Mental signs.— Sluggishness at times, alternating with sparkling wit. Irritability which grows worse at any slight opposition. Moodiness generally. Inability to concentrate; forgetful; easily tired; lack of confidence; heavy dullness in the morning which wears off as the day progresses. Require much sleep.

Hair. — Usually coarse and dry. Tendency to come out. Likelihood of dandruff. Hair lacks brilliance and looks dusty.

Head.—Liability to generalized dull aching on slight effort. Headaches usually frontal or occipital.

Eyes.— Eyebrows tend to sparseness, especially the outer third. Scaliness of skin under eyebrow. Puffiness of upper eyelid, particularly outer half. Sparse eyelash growth. Orbit often seems sunken, enopthalmic. Dull expression generally to eye. Iris pigment usually hazel or grey green. Rarely a clear color as brown or blue. Pupil tends to be narrow.

Nose.— Tendency to rhinitis. Crusts form frequently.

Ears.— Scales form easily along external auditory meatus.

Mouth.— Lips tend to dryness and cracking. Tongue thick and stubby. Teeth often leave their imprint along margin.

Teeth. — Heavy, soft, easily becoming carious. Tend to yellowish stain. Liability to pyorrhea.

Tonsils. — Tonsilitis attacks are frequent. Tonsils usually enlarged.

Respiratory system. — Frequently acquire cold and difficulty in recovery. Tendency to winter bronchitis which usually has associated a productive cough. Adenoid tissue overgrowth likely in children.

Cardiovascular system. — Cardiac rhythm steady and sluggish. Not affected easily by physical or emotional stress. Rate tends to be slow — around sixty. Systolic pressure unchanged, but pulse pressure usually less than normal. Extremities usually cold, may be damp. Poor capillary circulation as shown by slow refilling of skin capillaries after pressure. No stimulation reaction experienced after cold baths. Patient usually takes only warm or hot baths. Patient feels much better in warm weather. Winter often makes him feel utterly miserable. Vasomotor skin reaction and pilomotor skin reaction very sluggish. Both may be absent. Temperature usually subnormal.

Digestive. — Appetite usually not large, but at times it is extreme, but even at these times it is easily satisfied. Patient experiences times when he craves sweets. All food agrees with patient. Tendency to tasteless, gaseous eructations after meals, and meteorism and offensive flatus. Tendency to thickening of rectal veins with bleeding. Tendency to gain weight rapidly. Desire to sleep after meals.

Urinary. — Tendency to polyuria. At times slight traces of albumin and sugar appear. Indican frequently excessive. Nocturnal enuresis often present.

Skin. — Dry. Thick. Tends to scale easily and often shows psoriatic and eczematic patches. Tendency to small warty growths. Perspires with difficulty. Yellowish earthy color. Fingers and toes often seem cyanosed. Fragility of nails, which show ridges and thickening.

Skeleton. — Relaxation of ligamentous structures. Crackling noises on motion of small joints.

Conclusions

Having determined that the patient can be included in this symptom group, and, although one cannot, as yet, define laws for such inclusion, the careful clinician will soon be able to tell easily whether the patient presents enough of the above physical signs to warrant this diagnosis, the problem then to be met is that of the therapy. This is a problem of readjusting and accelerating the individual's thyroidal tonus to the normal.

I begin with doses of one tenth grain of thyroid extract, given on an empty stomach, either in the morning on awaking, or on retiring at night. This dose is given once a day for a week and the result noted. It is important to mention here, that although the constipation may be unchanged, one or more of the other symptoms which the patient revealed, which are equally important in their thyroidal bearing as is the constipation may be bettered or cured. If this is the case, repeat the same routine another week for it means improvement generally. Both patient and physician must be willing to travel slowly. The constipation, being so pronounced and gross, may persist to the last. Do not be discouraged by slow results.

To return to the therapy: If the small dose has no effect it should be increased in quantity, but administration once a day as before is all that is necessary. From one tenth grain go to one half grain, then to one grain and so on. The proper quantity will be found, but what it will be is impossible to predict.

I have met the following extremes: A child of twelve was perfectly well for six months after three doses of one tenth grain, whereas, on the other hand, a man of forty required fifteen grains each day which were taken for weeks at a time without the slightest toxic sign.

I have not been able to determine that the product of any one manufacturer excels that of another, but as a general rule, it is best to get the freshest preparation as all animal extracts seem to deteriorate with age.

While under this regime the patient lives as he wishes. Of course, any cathartic or laxative medication is strictly forbidden. If the bowel remains absolutely inactive for thirty-six hours, small saline enemata may be used. The patient is not placed on any dietary restrictions, he is told to live as he pleases and to forget his troubles.

As soon as the intestinal action is normal, stop the thyroid extract. Then give no further medication unless there should be a symptom return, in which case the treatment routine is repeated.

Our task is not the creation of an atmosphere replete with restrictions in which the sick individual can live, but the adjustment of the patient to his normal environment by improving the coördination between his glands of internal secretion.

* *New York Medical Journal*, Feb. 14, 1920.

Comments on the Function and Clinical Uses of the Pineal Gland*

By William N. Berkeley, A. B., Ph. B., M. D.

* * * An exhaustive treatise on the morphology, evolutionary significance, pathology, and clinical relations of the pineal gland is in course of publication by Tilney and Warren. * * * While relatively more active in early life, it does not, as supposed by some, atrophy with sexual maturity. It evidently retains through life a fairly definite size, and any function it may possess in infancy is probably not altogether abrogated in adult years.

As a matter of some clinical and diagnostic interest we may note, parenthetically, the observation of Schullet, of Vienna, that after calcification of the gland has occurred, pineal shadows will appear in profile x-ray photos of the skull — about 1 cm. behind and 3.5 cm. above the external auditory meatus. * * *

Whatever be its evolutionary relations the opinion is constantly gaining ground among clinicians that physiologically it is a true organ of internal secretion. Supporting this conception there are both experimental and clinical data, some of which I shall now proceed in an entirely informal way to set forth.

My interest in the pineal body dates back a number of years, to a time when Dr. C. L. Dana, of New York first called my attention to a case of pineal gland tumor reported by Von Hochwart and suggested that some research work on the subject might prove fruitful. Von Hochwart's case was that of a boy of five years, who had projectile vomiting and choked discs — indicative, of course, of cerebral tumor. It was not, however, the presence of a cerebral tumor that was so noteworthy, but that the patient showed a physical and mental precocity far beyond his years. He was as large as a boy of fourteen, had a bass voice, a growth of pubic hair, and concerned himself much with ethical problems and immortality.

Von Hochwart's case has not remained isolated. A succession of tumors of the pineal gland has been subsequently reported in the foreign neurological journals, and by Bell, Warren, Tilney, Dercum, and others in the *Journal of Mental and Nervous Diseases* in this country. The symptomatology of them all has been similar, and nowadays signs of cerebral tumor in the region of the corpora quadrigemina, concurrent with abnormal growth of the body, early appearance of axillary and pubic hair, and remarkable sexual and mental precocity, are grouped definitely as the "pineal syndrome."

To recur, however, to Von Hochwart's case, the autopsy revealed a cellular tumor of the pineal gland. Von Hochwart and his colleagues advanced the view that the pressure of this tumor had inhibited the growth and secretion of the pituitary. But it seemed to Dr. Dana and myself simpler and much more probable that the pineal secretion itself by reason of its increased amount had brought about the extraordinary mental and somatic growth above described.

Working upon this hypothesis for several years, under Dr. Dana's constant and helpful supervision, and with some financial assistance kindly granted us by the Trustees of the Rockefeller Institute, I was able to show that preparations of pineal gland, gotten perfectly fresh from calves and young cattle, accelerated the somatic growth of kittens, rabbits, and guinea pigs to a marked degree, and that a number of backward children, without organic stigmata, to whom the gland was administered for a sufficient period — usually three to six months — made an advance in mental age considerably in excess of any previous progress for a like period. The work with the children was conducted not only by Dr. Dana and myself, but by various other observers. Details of the research may be found in the paper finally published by us in the *Medical Record*. This account attracted more than usual attention, if I may judge from the numerous scientific discussions and experiments that have followed. Some (Ruggeri, Biondi) have touched only on the histopathology of the gland, and this will not be discussed here. McCord was able to confirm fully, and to amplify our feeding experiments. Dandy, operating on puppies, from the brains of which by a new surgical method he claimed to have successfully removed the pineal gland, reported that growth proceeded, and sexual maturity appeared as well without the pineal gland as with it. G. Horrax, who made extirpation experiments on rats and guinea pigs, claimed that pinealectomy accelerated growth and sexual development in the animals operated on. Fenger extracted pineal glands, and with his extracts was unable to get results of any kind distinguishing his subject animals from the controls.

As regards Fenger's work the chemical details of his extraction processes are not clear enough to admit of a definite opinion being expressed:

---

* *Medical Record*, Jan. 3, 1920.

but it is plainly impossible that the observations of Dandy and Horrax should both be true. I am disposed to think that excision experiments, at all events those of the character so far adopted, involving a profound disturbance of the circulatory and anatomical relations of almost the entire brain, will have to be left out of the story and that feeding observations and clinical experiences should be given exclusive attention.

Recurring, therefore, to the clinical study of the pineal body, I should like to report summarily that my later work with the gland in backward children in private practice, has continued to be gratifying and satisfactory. The only requirements are that the child should be properly cared for in an educational way, and that the remedy should be continued for a long period— perhaps years instead of months and weeks. There are some fathers and mothers who demand a cure for their abnormal children in a week: for such parents there is nothing ahead but disappointment.

I have brought with me here tonight (there will not be time to read them) notes of six cases of small boys and girls recently in my care who have done very well indeed on pineal gland, their mental progress, in the opinion of their parents, physicians, and teachers having been notably accelerated.

In the care of all such cases one must continually bear in mind that "mental backwardness" in a child is a vague term, covering an infinite multitude of unknown conditions. A careful and minute examination of every feature of each case must be repeatedly made: for outside of the cretins and Mongols, but few generalizations are possible. The prenatal history is often important, and, of course, the character of the labor, and the baby's nutrition and food must be carefully looked into. The child's mental age must be rather accurately determined, and the special senses, the tonsils and adenoids, the teeth (both present condition and stage of eruption), the skin, the blood pressure, the shape of the hands and feet, the quality and distribution of the hair, the relation of the weight and height to the age, are all very important. X-ray photos of the skull showing up the pituitary fossa, and giving possible indications of cysts, neoplasms, or hemorrhages of the brain, are almost indispensable. And, of course, a serological examination of the spinal fluid should be a routine measure, where the parents can be got to consent to it.

When all this work has been carefully done, it will soon become evident to the attentive student — it is no discovery of mine — that glandular deficiencies often do not come singly, and pineal gland must often be tentatively combined with other secretions. Minor grades of hypothyroidism should be specially suspected, and a dry skin, cold extremities, obstinate constipation, excessive mental hebetude, irregular and imperfect eruption of the milk teeth, low blood pressure — one or all of these may be remarkably intractable till thyroid is added to the formula. When the physical as well as mental growth is retarded and there are changes in the size of the sella, or increased carbohydrate tolerance, or great obesity, or a systolic blood pressure below 50 mm., the anterior or the middle part of the pituitary, or both, should be added. When the patient is a boy and has very minute and soft testes (a common occurrence), testis should be given. Sometimes several of these conditions coincide, and a pluriglandular formula of pineal, pituitary, testis (or ovary for girls), and thyroid—all in minute doses—may be tried, often with the most gratifying results.

An important cautionary note should be added as to where such pluriglandular prescriptions — or for that matter prescriptions for any kind of internal secretion — should be procured. One young medical friend telling me recently of his ill success in a certain case said he had sent his patient's mother with the prescription to the nearest pharmacy, directing the pharmacist to "use the very best materials he had." This is something like asking the milkman's advice in making up a formula for a baby with a chronic diarrhœa. There are now several New York wholesalers who specialize in internal secretions, and in properly prepared pluriglandular formulas; and if the medical attendant hopes for results in any wise commensurate with his thought and effort in diagnosis he should not be satisfied with any gland preparation unless he is sure it is absolutely fresh and obtained from a well-known and reliable source.

As a means of speeding up the sluggish cerebral chemistry of many backward children, I believe that pineal gland will ultimately become a standard remedy, but the cases must be selected with reasonable care; permanent organic damage to the child's brain is usually an absolute contra-indication.

As a corollary to the clinical use of pineal gland in accelerating the chemical movement of the brain in the backward child, it has appeared to me justifiable to try it in premature decay of the mental powers in old people. I have found that while it will not make over hardened arteries or a dilated heart, it will quicken the slowed-down mental processes of old age, improve the memory, and produce a remarkable cheerfulness and sense of well-being. Some of my elderly patients have taken it for years, and decline to be without it.

In conclusion of this rather disconnected discourse, I must not omit to mention that W. Timme has recently offered some interesting evidence toward proving that progressive muscular dystrophy is an endocrinopathy, and that the pineal gland is the organ at fault in such cases. The paper is too long to be quoted at length, but is worthy of serious consideration. The argument is based partly upon clinical signs, partly upon the appearance of pineal shadows in the x-ray photos of the skulls of the patients reported, the said patients being, it is claimed, all too young for calcification to have developed.

BRIEF ABSTRACTS

Influence of Pituitary Extracts on the Genital Tract. — Robert T. Frank, M. D., New York (*Jour. A. M. A.*, Dec. 6, 1919). Various results have been obtained by investigators from the feeding of anterior lobe extracts. The growth-producing effect of hypophysis extract appears to be generally accepted in the literature. The author completed his experiments in 1917, and investigated the physiological properties of the lipoid constituents of the various endocrine glands and the effect of the anterior lobe of the pituitary body on the growth of the genital tract.

White rats were used as the experimental animals. At necropsy it was found that no concordant increase in size or in general body weight or in the genital organs ascribable to the glandular feeding was present. Irrespective of whether experimental animal or control, certain rats showed a greater increase of weight, the presence of corpora lutea in the ovaries, and enlargement of other internal genitals.

More extended experiments will be necessary before stimulation of the sex organs, particularly the female sex organs can be ascribed to the use of pituitary extract.

Pancreatic Extract in Gastric Cancer, M. Loeper (*Progrès Médical*, August 30, 1919). Loeper's results from the intravenous injection of pancreatic extract in the treatment of gastric cancer show a decidedly favorable action on some of the symptoms of gastric cancer. There was increased weight, number of erythrocytes, and antitryptic index. The treatment gives increased antiproteolytic power to the blood serum, and resisting power to the blood corpuscles. The general condition improves.

Placental Hormone, a Physiological Galactagogue. Bertha Van Hoosen, A. B., M. A., M. D., Chicago (*Illinois Medical Journal*, January, 1920). Dr. Van Hoosen gives the results of her experiments in the administration of placental hormone in ampoule form in 33 cases in which it was given before delivery. 36 control cases without placental hormone are also given. The interesting results of squeezing out the placenta and giving the blood per rectum immediately after delivery are also given. This was done on the theory that it might be possible that an autogenous hormone, if it could be so designated, might be more valuable.

The author's results show:

1. The placental hormone is a powerful stimulant to the secretion of the mammary gland, but that its effect is uite temporary and must be repeated at intervals to maintain its action.
2. The secretion of milk would be established on the first day, or at the latest, the second day if the placental hormone is administered in large doses previous to or at the time of delivery.
3. The discomfort of a sudden and violent establishment of the mammary function is avoided when placental hormone is administered.
4. Placental hormone will stimulate the mammary gland at any period during lactation.
5. Bovine desiccated placenta, administered by mouth, is our most satisfactory galactagogue.

Traumatic Shock and its Treatment (*American Journal of Surgery*, January 1920). Turck believes that traumatic shock is caused by toxins liberated from wounds. His experimental investigations on cell necrosis and clinical observations led him to this view. In trauma, the destroyed tissue undergoes autolysis through enzyme action and split proteins are liberated which are extremely toxic, and in large enough quantities cause shock. It is evident that the treatment should be the removal of the devitalized tissue, hence surgery in traumatic shock is more successful than antiseptics and drainage. Any agent capable of destroying tissue may be an etiological factor of shock. Chloroform or ether causes cell necrosis, and therefore produces shock or increases the amount already present. The traumatic shock syndrome follows whenever destruction of tissue takes place. The author's experiments indicate that the shock syndrome comprises two distinct phases: First, the toxins liberated by the disintegration of dead cells, and second, the marked splanchnic stasis.

Treatment in traumatic shock must aim, first to remove the blood stasis of the splanchnic area, and second, to neutralize the toxins which are poisoning the patient. To remove the blood stasis in the splanchnic area, heat is employed. The author advocates the use of small, thin, rubber hot water sacs, introduced into the abdomen during surgical operations. Where the abdomen is not open, the sac described is attached to a double recurrent rubber tube introduced into the stomach. The colon may also be used for heat application. Turck has for may years advocated the use of continuous irrigation of the colon in operative or accident cases and infections of various types.

The neutralization of the toxins resulting from necrosis is brought about by the employment of a specific immune horse serum, which may be produced by immunizing horses with human autolyzed tissue protein. A serum containing antibodies against human autolyzed tissue is the only logical treatment against the poisonous autolyzed tissue resulting from cell necrosis. The author states that although he considers surgery far superior to antiseptics in the treatment of traumatic shock. he does not advocate surgery in all cases. The treatment is both physical and biological, rather than surgical.

Lung Tissue as a Hemostatic. C. A. Mills (*Journal of Biological Chemistry*, Dec., 1919), investigated thromboplastic activity of various tissue extracts on the blood both intra- and extravascularly. He found that lung tissue extracts were far more active than the extracts of any other tissue, kidney coming second, and then heart, brain, spleen, thymus, testes, and skin, more or less in the order named. The remaining tissue extracts were weakly active as compared to lung, some of them showing very slight thromboplastic action. The author suggests that lung tissue would make a more efficient hemostatic than those in the market today, which are prepared from brain material.

Mills states that the strong coagulative activity of lung and kidney tissues, and to a lesser degree of skin, is suggestive of a possible protective mechanism against hemorrhage.

The investigation of the nature of the active hemostatic principle of lung extract is being carried further and will form the subject of another paper.

The Calory Value of Food Not a Reliable Measure of Its Value. In a timely paper, Henry Dwight Chapin (*Jour. A. M. A.*, Dec. 1919) says that the practising physician is required to solve numerous problems which call for the selection of food of the right physiologic value for a given individual. What may be the right physiologic value for one may not be suitable for another. It has been conclusively shown that in practise the caloric value of food is not strictly indicative of its nutritive value, but it has not been shown why this is so. With the recognition of the fact that an animal body is not merely a furnace in which food is burned, but that a long series of changes in the food takes place, it is not difficult to see why practical results cannot be obtained with food valued only by the oxidation properties.

He points out that heat or energy may be produced by chemical cleavage, as well as by oxidation. Heat may be a degradation of energy, and in the human organism it is an excretion. Heat measurement alone is not a safe guide for the calculation of food values. This is especially true at the beginning of life when growth is the all-important factor. The foods that build rather than those that readily undergo oxidation must be properly gaged if we are to have healthy development. A false theory does harm in that it points in the wrong direction and it is a question whether it is not time to weigh carefully the calory theory of feeding and restrict or partially abandon its use. To take its place, a system of teaching must be constructed based on the knowledge of the physiologic properties of the various food elements and the fact that there are mixed types of metabolism.

The Spleen and Resistance. Morris and Bullock (*Annals of Surgery*, Nov., 1919). These workers made an investigation to find out the part played by the spleen in combating infection. They took 36 young brindle rats, weighing from 50-100 grammes each and splenectomized them under anæsthesia. Another series of 36 had one testicle removed. Both series were active and healthy on the day following the operation. They were exposed to chance infection from laboratory contagion and kept under observation for several months. The death rate in the splenectomized animals was 80.5% as compared with 38.9% in the controls.

The authors deduce from these findings that the splenectomized rats were more prone to contract rat plague, and that having contracted it, they showed less resistance to its ravages. Other experiments along similar lines brought similar results and the authors conclude as follows: While rats may get along fairly well without the spleen in the absence of any infection, the reverse is the case when the organism is put to the strain of resisting acute bacterial invasion. The inference is that the spleen normally aids tremendously in resisting infective processes in rats, and that its removal temporarily robs the body of its resistance.

The Influence of Splenic Extract on the Number of Corpuscles in the Circulating Blood, Ardrey W. Downs and Nathan B. Eddy (*The American Journal of Physiology*). The authors say that their experiments were undertaken in order to determine the effect on the number of both red and white corpuscles in the circulating blood of injections of splenic extract. They believe that such a determination must throw some light on the possibility of the presence of an internal secretion of the spleen capable of affecting formation or destruction of blood corpuscles.

The experimental animals were rabbits. After an initial count of both red and white corpuscles, subcutaneous injections were made of splenic preparations. Subsequent red and white corpuscle counts were made at half-hour intervals, and a final count four or five hours from the beginning of the experiment. The results of ten experiments in one group were practically the same — a slight reduction in the red corpuscle count of short duration, a prompt reduction in the number of white corpuscles followed in several hours by a leucocytosis. In similar experiments in which precautions were taken to use a protein-free splenic preparation, the red corpuscle count also decreased following the injection. An increased leucocyte count of brief duration is recorded. The authors conclude that the effect of the erythrocyte count at least is a specific effect of the splenic preparation. This decrease of red corpuscles and transient increase in leucocytes occurred after the use of desiccated and fresh extracts of spleen.

The authors believe that their results show the existence in the spleen of two substances — one a direct hemolytic agent acting particularly upon the older and less resistant corpuscles, the other an agent stimulating the production of new corpuscles by the bone marrow. They conclude that subcutaneous injections of protein-free splenic extract is followed immediately by a decrease in the number of erythrocytes in the circulating blood; that the decrease is temporary and is probably due to direct hemolytic action of the splenic agent; and that the decrease is frequently accompanied by a very transient increase in the number of white corpuscles.

Glycosuria in Three Cases of Chronic Nephritis with Edema but with only Slight Nitrogen Retention.—Victor C. Myers and Ludwig Kast (*Journal of Biological Chemistry*, March, 1920). "Renal diabetes" has been the subject of much discussion since Lépine in 1895 postulated the existence of this condition in which the glycosuria is the result of renal disease and not due to hyperglycemia. About thirty cases have been recorded. Renal diabetes has been compared with phlorizin glycosuria. The cases reported by the authors seem to be analogous to the glycosuria of uranium nephritis. In all three cases reported, there was marked proteinuria and edema but little nitrogen retention. One of the cases gave normal blood sugar, but the other two showed a mild hyperglycemia. In one of these the glycosuria was shown to be independent of the mild hyperglycemia. Sugar was found in the urine in quantities from zero to slightly over two per cent. Most frequently it amounted to about five-tenths per cent.

The Treatment of Thyrotoxicosis by Means of Roentgen Ray. — George W. Holmes, M. D., and Adelbert S. Merrill, M. D. (*Jour. A. M. A.*, Nov. 29, 1919).

The authors' experiences during the past five years in the roentgen-ray department of the Massachusetts General Hospital, during which they treated 262 cases of thyrotoxicosis, is sufficiently encouraging they believe, to warrant a more general use of this agency in the treatment of this condition.

It has been shown that it is possible to destroy the glandular structures by subjecting them for a sufficient length of time to the roentgen ray or radium. It is also generally known that the action of this form of light is most destructive to the higher organized type of cell and that the tissues of the lymphatic system are particularly vulnerable. If these statements are true and the amount of irradiation sufficient to destroy the thyroid gland is not greater than that which will produce an injurious effect on the skin, it should be possible to remove all of the glands by means of irradiation and produce results similar to those of surgery without the dangers incident thereto.

The authors divide their cases into four groups:

1. Patients in whom very definite benefit ensued, apparently as the result of treatment, and are clinically well.
2. Patients in whom there was a definite improvement but who still manifested some evidence of disease.
3. Patients in whom there was no change under treatment or who became definitely worse.
4. Patients in whose cases fairly complete data were obtained; at least one basal metabolism record was made and sufficient time had elapsed to warrant a definite opinion as to the final result. The cases in this group are selected from the other three.

Under group 4 a fairly complete study of 36 cases is comprised. Seventeen of the patients were perfectly well, while thirteen were improved, and in four cases the diagnosis was incorrect as proved by the metabolism determination. One patient was operated on without relief; two had recurrence of symptoms, and in one case myxedema developed as a result of over treatment. One patient died from unknown cause during treatment.

During the last three years of the period most of the work was done with an interrupterless machine, Coolidge tubes being used. The rays were filtered through 4 mm. of aluminum and 1 mm. of leather.

The dangers incident to the treatment are that the function of the thyroid gland may be destroyed and hypothyroidism produced. Telangiectasis may occur. Toxemia may be increased to a dangerous degree by the first treatment.

In most of the cases reported, decided improvement was noted twelve months after treatment was begun.

The authors conclude that it is possible to decrease the activity of the thyroid gland and probably to destroy its glandular structure by exposure to the roentgen ray.

Roentgen ray treatment when applied in cases of thyrotoxicosis produces a relief of symptoms and shortens the course of the disease.

A study of the basal metabolism before, during, and after treatment is of the greatest importance both as a means of diagnosis and as a check on the amount of treatment to be given.

The roentgen ray, accompanied by rest, should be tried in all cases of thyrotoxicosis and should be continued for a sufficient length of time to destroy at least the thymus before resorting to surgery.

The Influence of the Thyroid Gland on the Formation of Antibodies. — J. Koopman, The Hague (Holland), (*Endocrinology*, July-Sept., 1919).

Koopman made experiments to increase the amboceptor titer in rabbits. During the war rabbits were scarce and it was found that well fed and apparently healthy animals could be injected "ad infinitum" without giving a serum with satisfactory hemolytic power. The formation of hemolytic amboceptor may be considered a special case of antibody formation. The formation of antibodies is a regenerative process largely under the control of the thyroid gland. In the case of one rabbit the titer was but 1.100 after 15 intravenous injections of 1 c. c. of a 5 per cent. emulsion of sheep corpuscles.

At first intra-abdominal injections were made of fluid expressed from the fresh glands of the cow and later of the pig. After some weeks the fluid was administered by mouth. Before beginning the experiments the titer was 1.100 and during treatment it increased 1.1200. Three of the four offspring of this male rabbit gave serum with a titer of from 1.3000 to 1.3600.

Koopman suggests the desirability of the investigation of the formation not only of hemolytic amboceptor but also of agglutinins, antitoxins, bacteriolysins and other antibodies.

The Rational Therapeusis of Exophthalmic Goiter. — Israel Bram, M. D., Philadelphia (*Endocrinology*, Oct.-Dec., 1919). After a lengthy review of the subject, Bram concludes that Graves' disease is gradually becoming recognized as a disease strictly non-surgical in nature and requiring non-operative remedial measures. The disorder is one strictly outside the domain of surgery unless dangerous pressure symptoms arise or malignant changes set in.

Careful non-surgical management is capable of completely and permanently curing the great majority of cases of hyperthyroidism. The occasional exception not responding to non-surgical measures is not an instance of genuine Graves' disease, but is one of malignant degeneration of the thyroid gland, a case of toxic symptoms superimposed upon a long standing non-toxic goiter, or a case brought to the clinician's attention in a moribund condition. Bram, in unison with others interested in thyroid therapy, does not hesitate to conclude that he has been able to cure every case of primary Graves' disease in which a fair degree of co-operation was obtainable; this was accomplished in from six months to two years, depending upon the exigencies of the case treated. Strict individualization of the case in hand is the dominating principle of treatment. The proper medical attendant, the proper social atmosphere, and the right kind of dietetic, hygienic, medicinal, psychotherapeutic, electro-therapeutic and other measures properly applied for the required length of time should yield permanent cure.

A Contribution to the Treatment of the Incoercible Vomiting of Pregnancy, Lacourbas (*Thèse de Paris*, 1919, No. 71). — The author deduces from five observations, previously reported by Potiet, that where the vomiting was so serious as to lead to death, it was found, on autopsy, that there were lesions of the corpus luteum.

He considers functional insufficiency of this gland as the prime factor in the auto-intoxication that causes this vomiting. After reviewing the works on the subject, he gives five unpublished cases, in which administration of corpus luteum extract, together with a deintoxicating diet, led to a cure.

Gastric Disturbances of Endocrine Origin. Hernando (*La Medicina Ibera*, Madrid, Sept. 27, 1919). After a long discussion of the subject, Hernando comes to the following conclusions:

1. The glands of internal secretion exert an influence on the digestive apparatus in two ways: through the direct action of their products of secretion upon the muscular fibre and the digestive glands, or through the intermediary of the vegetative nervous system.

2. In the development of every disease, there must always be a certain pre-disposition, for a sound organ should be able to resist all ordinary attacks without being affected, a degree of resistance which the man of today has not attained.

3. Stiller's asthenia (Glenard's splanchnoptosis), the appropriate soil for the development of many digestive disturbances, may be considered, together with other constitutional conditions, the result of congenital disturbances of the endocrine glands and the nervous system, which are the great regulators of all the phenomena of the organism.

4. Modifications in the functioning of the endocrine glands may be the cause of disturbances, of the secretion of gastric juice.

5. Of these disturbances, the hypo-secretory is more frequent than the hyper-secretory type, no doubt because the former are often the manifestation of a congenital constitutional condition, which is so frequently met with in endocrinopathic patients, just as they may be the result of a disease (cancer, syphilis, tuberculosis, etc.) which induces the endocrine lesion or the cachectic condition of the patient when the disease is advanced.

6. One finds, however, many cases of hyperchlorhydria in patients with hyperthyroid symptoms (the extract of normal thyroid has a stimulating action upon the gastric secretion), and in others with suprarenal insufficiency (the extract of suprarenal capsules has an inhibitory action upon the gastric secretion).

7. Our clinical observations and the result of the experiments of other investigators permit us to establish a connection between suprarenal insufficiency and gastric ulcer.

8. Patients with suprarenal insufficiency, as a rule, combine conditions favorable for the development of gastric ulcer. Among these is the lymphatic condition, disturbances of the vegetative nervous system, persistence, and sometimes even an augment, of hydrochloric acid in the stomach, and finally, the lessened resistance towards infection.

9. Although we have noted gastric ulcer in patients with advanced symptoms of suprarenal insufficiency, it is not unlikely that slighter degrees of insufficiency may together with other causes (endocrine, infection, etc.) play an important part in the pathogeny of ulcer of the stomach, as is proved by the frequency with which one meets with endocrine stigmate in patients with gastric ulcer.

10. The harmful effect of fatigue and emotion upon patients with ulcer and hyperchlorhydria, may be explained by the suprarenal exhaustion which they induce, and hence, the beneficial effects which in these cases, follow rest and the use of suprarenal extracts.

A Very Constant Symptom of Hyperthyroidism. — Maranon (*Revista Espanola de Medicina y Cirugia*, November, 1919). Some years ago Maranon pointed out the constancy and value of the following symptom of hyperthyroidism. This symptom consists in an erythema induced by slight friction of the skin of the neck with the fingertip; this erythema is more marked here than in the adjacent regions; and when there is a goiter it may be localized, or be more marked, on the skin covering the tumor; or if the latter is to one side, it may be more marked on that side. This erythema may be uniform, or irregular, smooth, or accompanied by swelling. It is observed in 87% of cases of hyperthyroidism in all its forms, even those characterized by a scarcity of other symptoms, and has no relation to any marked degree of hyperthyroidism, but rather to nervous symptoms, and particularly sympathicotonic symptoms; to the female sex, and to youth, and to the menopause.

The author believes that he is the first to describe this symptom, which must not be confounded with the readiness with which cutaneous hyperemia may be spontaneously produced.

The pathogeny should be referred to a sensitization of the vasomotor nerves, from excessive thyroid secretion, or possibly through a qualitative change; this action must be induced by hormones passing from the thyroid gland to the skin through the blood, and not through nervous mechanism, since it is especially manifest in the thyroid region itself.

A Test of the Digestion of Nuclei, and the Diagnosis of Pancreatic Insufficiency. — Marcel Labbé (*Bull. et Mem. Soc. Med. des Hop. de Paris*, July 31, 1919). Labbe reviews the work of Schmidt on the digestion of nuclei in the diagnosis of pancreatic insufficiency. The nuclein of cellular nuclei has the property of being digested by the pancreatic juice alone, and not being digested by gastric or intestinal juice. Labbé employed this method in 111 cases and gives the results. He concludes that the test of the digestion of nuclei is of real interest in the diagnosis of pancreatic insufficiency. He believes it is necessary, to avoid error in interpretations, not to base a diagnosis exclusively upon it, and to accept no results that do not agree with the clinical findings or the chemical examination of the products of digestion.

Diabetes Insipidus and the Hypophysis. — Prof. Lereboullet (*Le Progrès Médical*, Sept. 13, 1919). This article discusses the connection of diabetes insipidus and the hypophysis. In a considerable number of cases diabetes insipidus appears to be connected with a lesion of the hypophysis. Lereboullet has employed injections of hypophyseal extracts with success. In view of his experiments, he states that it cannot be asserted that polyuria in diabetes insipidus is a direct hypophyseal symptom, but that nevertheless a hypophyseal lesion is present in a great number of cases, and that extracts of the posterior lobe have a curative, though temporary, effect.

Arterial Tension in Grippe. — L. Tixier (*Paris Médical*, July 5, 1919). Tixier states that grave cases of grippe have appeared to be cases of hypertension of average intensity, but not leading to important functional circulatory disturbances. Tixier states that, as a general rule, grippe patients do not seem to die from heart involvement. There is, however, a certain disturbance of tonicity of the cardiac muscular fibre evidenced by respiratory oscillations and by the feeble action on the heart of tonics which are usually active, such as camphorated oil and digitalis. At necropsy he never observed sufficient heart change to cause death. Suprarenal insufficiency is indicated by the undeniable hypotension, intense attacks of general vaso-dilation, asthenia, sometimes accompanied by vomiting, and the frequent presence of Sergent's white line. Intensive adrenalin medication appears to have beneficial action in desperate cases. This action is due probably to stimulation of the sympathetic system, of which it is the specific stimulant. It appears that in grave cases of grippe, where the patient offers no resistance and the cardio-arterial reaction is as defective as the immunizing action, that the great sympathetic was perhaps more than other organs destroyed by toxemia. The evidence of its exhaustion is clear from a cardio-vascular viewpoint; hypotension and vaso-dilation. This may possibly partially explain the rapid exhaustion of young organisms which seem as though they should offer resistance, but which succumb within a few days, almost without a struggle, overcome by the general effects of the toxemia, rather than by the apparent and sometimes trivial pulmonary, renal or cardio-vascular lesions.

Glandular Insufficiency in Children's Diseases. — Leon Tixier (*Le Bulletin Médical*, Nov. 8, 1919).

The minor symptoms of thyroid insufficiency are much more interesting to trace, for they are commonly observed in pediatrics. They are usually present, associated in various ways, in young girls or schoolboys of 10 to 15 years of age.

Frontal headache, or occipital neuralgia, of a hemicranial type, worse in the morning, and preventing all study. Great fatigue is experienced in the morning as soon as they begin to work; overpowering drowsiness after meals, and intellectual work becomes very toilsome. The mental equilibrium shows a tendency to become unbalanced; children cry on the least provocation.

Disturbances of the circulation are usual; hands pale or blue, extremities cold. A slight tendency to obesity is noted, especially in girls.

Incontinence of urine is not exceptional, but to us it appears to constitute a sign of thyroid insufficiency only when it is associated with the foregoing symptoms. It appears even more questionable to refer to this cause, as do certain authors, the transient oedemas, the tendency to ichthyosis or to scleroderma, constipation, headaches and too abundant and painful menstrual discharge. It is chiefly in these conditions that one must avoid diagnosing thyroid insufficiency, unless one has a combination of indisputable proofs.

The treatment of thyroid insufficiency should be prescribed in the form of dry extract, which is obtained commercially in the form of tablets or lozenges, and administered to the amount of from 1/6 gr. to 1 gr.

To a child under five years, one may give 1/6 or 1/3 gr. a day, in two doses or 1/3 gr. every two days. Above that age, one may give 1 gr. every twenty-four hours. Between 10 and 15, 1½ to 2 grs. are quite large amounts, which demand special watchfulness on the part of the physician.

At first the child should be placed on a milk and vegetable diet, and take a saline purgative twice a month.

The parents should always be told to take the pulse every morning and evening at a regular time (standing up and lying down), and the rectal tem-temperature. If the pulse-beats reach 104 to 110, if the temperature rises to 38 C. or thereabouts, we do not have to wait for alarming symptoms; violent headache, dyspnea, trembling, a tendency to swoon — in order to suspend the thyroid medication.

It is not unusual to see obese patients, who, without medical surveillance, had taken large amounts of thyroidine for some time, come and consult us because they had grown thin, had palpitation, dyspnea and exophthalmia; one notes in them, tachycardia and enlargement of the thyroid.

In a majority of cases, several weeks treatment suffice to induce temporary or complete disappearance of the minor symptoms of thyroid insufficiency.

In pediatrics, hypophyseal insufficiency is certainly much rarer than suprarenal insufficiency. One should, nevertheless, seek its symptoms carefully during the course of grave maladies, so as to counteract them with an elective organo-therapeutic treatment. Two groups of symptoms betray the sick condition of the pituitary gland, cardio-vascular and urinary symptoms. Tachycardia and oliguria are symptoms of prime importance. In addition, patients sometimes experience a distressing sensation of heat, insomnia, asthenic phenomena.

(Continued next page.)

A New Lease of Life

When a patient is run down, has failing strength, prostration after exercise, cold hands and feet, with perhaps anæmia, constipation, want of attention to business affairs, weakness of memory, weak will-power, inability to perform mental work, incapacity of decision and other symptoms that are associated with a run down condition, it may be confidently asserted that the function of the dynamic glands of internal secretion is below par.

This condition may be more or less persistent or may occur at intervals, just as almost all of the constitutional psychoses are dominated by a periodicity. There may, in fact, be a melancholia of the body just as there is a melancholia of the mind. In these cases physical effort is almost impossible, there is a well defined physiologic laziness. Such conditions as these afford a fine field for pluriglandular therapy.

Hormotone is a preparation that imparts the necessary physiologic "kick" for such cases. Patients take on a new lease of life. They sleep better, eat better, in many cases their constipation is overcome, and they get a feeling of self-confidence that enables them to battle anew with the problems of every day life. Hormotone institutes and maintains normal function of the suprarenals and the glands associated with them, the thyroid, pituitary and the gonads. The glands form what has been termed the adrenal system and they furnish to the blood what have been very properly termed the dynamogenic hormones. Run down conditions and the lowering of mental and physical virility are accompanied by, and are probably due to, a deficiency of these hormones. Thus a perfect hormone balance is essential to the maintenance of health and to the restoration of a run down condition. Hormotone provides it. — Advertisement.

If the hypophyseal insufficiency is not restored, growth is retarded and trophic disturbances are noted, as well as psychic disturbances with slow mental development.

The treatment of hypophyseal insufficiency in grave maladies, is based not alone on histological findings, on the results of organotherapeutic treatment, but also on this fact, that hypophyseal extract has an undeniable action upon the circulation. This extract relieves arterial tension; its effect is more lasting than that of suprarenal extract. Under its action, the pulse becomes less rapid; a significant polyuria is the result of dilatation of the renal vessels.

Dry extracts, made from beef hypophysis, more rarely from calf or pig, are employed in preference to injectable extracts. The extract includes almost always the entire gland, sometimes only the posterior lobe; in the latter instance, the action is stronger. The daily amount is 1½ to 3 grs., made into two doses, and taken morning and evening. The medication may be continued without ill effects, for eight consecutive days.

Suprarenal Insufficiency. — Experimentation unfortunately does not permit us to correlate as completely as in thyroid insufficiency, the clinical and the experimental findings.

However, there are a certain number of syndromes which are indisputably connected with progressive destruction, or with insufficiency of these glands.

The Addisonian syndrome is almost always the result of a more or less complete destruction of the glands through a tubercular process.

Melanodermia or pigmentation is the symptom which first attracts attention, the pigmentation of the skin precedes the pigmentation of the mucosa.

Asthenia is an early symptom. Digestive disturbances are prominent: anorexia, slow digestion, nausea, vomiting, diarrhœa. The pulse is rapid, hypotensed. Moderate anæmia. Sudden death is a common occurrence, it may supervene in progressive cachexia. Hasty death with abdominal pains and a pseudo-peritoneal, or a pseudo-meningitic syndrome, as in very acute toxic poisoning, is rather special to total renal insufficiency in children.

Suprarenal insufficiency in the course of acute diseases is comparatively frequent. Sometimes it occurs during a hypertoxic malady, as in certain forms of malignant scarlatina, for instance. The symptoms of functional insufficiency are scattered amid the symptomatic complex of malignancy: excessive tachycardia, tendency to cold collapse, very special asthenia.

Sometimes, and this is far the most frequent result, suprarenal insufficiency manifests itself in cardio-vascular disturbances. Tachycardia is at times excessive, the pulse sometimes arhythmic, beats from 150 to 200 a minute. Hypotension is in some instances so great that it is impossible to estimate it precisely. The maximum usually oscillates between five and seven.

The cardiac bruits are weakened, with a tendency to equalization of the two silences. It is no exception for the embryocardiac rhythm to be perceived perfectly distinctly. And yet, contrary to what occurs in the course of myocarditis, the area of cardiac dullness is enlarged, and cardiac dilatation, except perhaps in the dying stage, is not apparent. The liver, also, does not present the clinical characteristics of the cardiac liver.

Suprarenal asthenia always imparts to children an appearance which is essentially characteristic; they remain lying stretched out on the bed without moving; they are extremely weak, dread the slightest change of position, refuse to speak, to drink. Sometimes they remain in a condition of dozing, interrupted by partial delirium.

Some children have pain in the epigastrium, dull, deep-seated, and aggravated by palpation. These are mistaken sometimes for peritoneal pains, but nevertheless, the parietal structure is never affected.

Sergent's white line is present in a certain number of cases.

Bazogen for Malaria

Each five grain tablet contains spleen, pancreas, thyroid (1/16 gr.), entire suprarenal substance (¼ gr).

Physicians who are interested in the treatment of malaria and who have the facilities for the treatment of a series of cases are invited to communicate with us, with a view of putting a liberal supply of Bazogen at their disposal for clinical demonstration. This offer is made without prejudice and with no obligations on the physician's part.

The dose for adults is two or three tablets three times daily after meals.

G. W. CARNRICK CO.
13-15 Laight St. New York, N. Y.

PHYSICIANS' LIBRARY

Book Reviews

Diet in Health and Disease. — Julius Friedenwald and John Ruhräh. 5th Edition reset. W. B. Saunders Co., 1919. Cloth, octavo. 919 pages. $6.00.

There are many books on the subject of diet and nutrition but that of Friedenwald and Rurah is conspicuously successful in presenting the accepted facts untinged by the views of food faddists, in a manner that makes it both a text book and a very practical working manual for the busy physician.

The physiology and chemistry of digestion and metabolism receive sufficient treatment to give clear comprehension of the practise recommended. There is an admirable discussion of foods in general, diet planning, diseases caused by errors in diet, etc. Infant feeding, milk modification, and the diet in special diseases receive adequate attention. The rapidly developing subject of vitamines is briefly but well discussed.

It should be emphasized that the book is distinctly practical — a physician may quickly find tables for milk modification, diet in a particular disease or instruction in dieto-therapy. A systematic reading from cover to cover will afford a splendid review and supplement to the physician's knowledge of diet and nutrition.

Physiology and Biochemistry in Modern Medicine. — J. J. R. Macleod assisted by Roy G. Pearce. 2nd Edition, 1919. Cloth, 903 pages. C. V. Mosby Co., St. Louis, $7.50.

The subject matter of this work is exceedingly well presented. The application of the principles of physical chemistry, biochemistry and physiology are clearly set forth. Many subjects, the development of recent years, such as colloid chemistry, are well presented and should be of unusual interest and value to the older practitioners. A careful reading of the work must prove of benefit to any physician. For those who are largely unfamiliar with much of the scientific matter, it is written in a style sufficiently simple to be easily comprehended. For the younger men it furnishes not only a valuable review but in a single volume much matter that ordinarily is found only in several books.

Real attainment as a clinician can only come through an ability to interpret symptoms in terms of physiology. Macleod's book is unquestionably one that will make for more rational and definite clinical procedure.

There are nine general parts:

I. The Physiochemical Basis of Physiological Processes.
II. The Circulating Fluids.
III. The Circulation of the Blood.
IV. Respiration.
V. Digestion.
VI. Excretion of Urine.
VII. Metabolism.
VIII. The Endocrine Organs or Ductless Glands.
IX. The Central Nervous System.

The great number of physicians who follow the excellent plan of reading once a year one good work on physiology will find this book one of the most instructive yet appearing.

The High Road to Health. — James E. Kelly, M. D., Dodd, Mead and Company, 1919. Cloth, 254 pages, $1.75.

Dr. Kelly's book is one that can be recommended to all persons, lay or professional, who desire simply stated rules for the preservation of health. The subject matter is based upon the personal experience of the author, who thirty years ago, was condemned to a sanatorium which he never saw.

Dr. Kelly sums up the six essentials of health as Perseverance, Air, Water, Exercise, Diet and Sleep. The importance of each of these is emphasized in several chapters. The chapter on Exercise is decidedly original and particularly good and well illustrated. It may appear to some readers that the chapter on Diet might have been more extended, but to the reviewer it seems to be adequately treated in a general work of this kind. The chapters on Habit, Constipation, Training and Social and Personal Poisons are well written and present the matter in a very interesting and practical manner.

The value of this book depends largely on the mental make-up of the individual who reads it. "Concentration on purpose is essential," says Dr. Kelly, and if the reader follows his advice in the right spirit, he will find in The High Road to Health a veritable cornerstone for an enjoyable life.

Books Received but Not Reviewed in this Issue

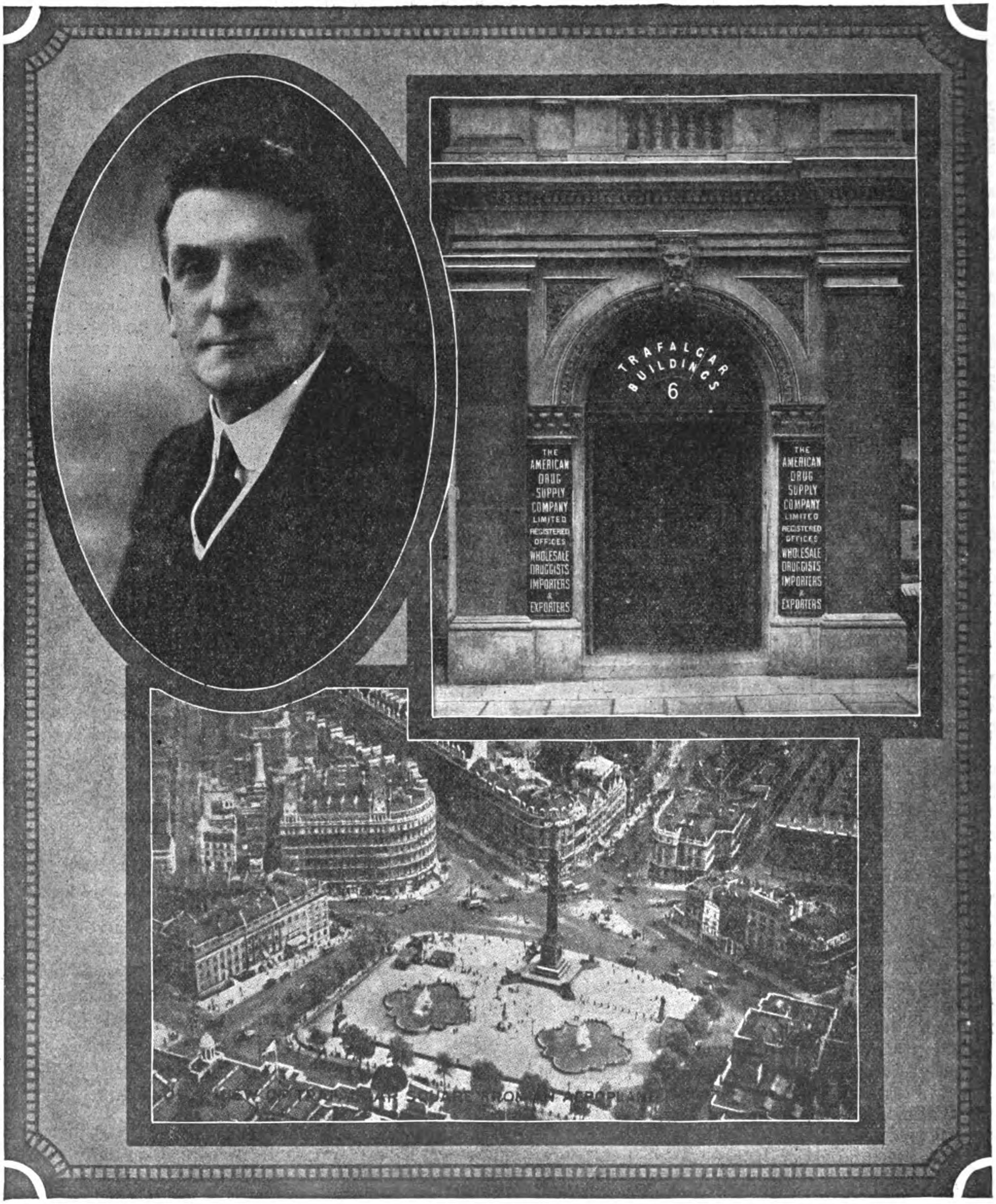
What to Eat and Why, by G. Carroll Smith, M. D. Second Edition. W. B. Saunders Company—1915. Octavo, 377 pages. Cloth. $2.50 net.

Food for the Sick, by Solomon Strouse, M. D., and Maude A. Perry, A. B. W. B. Saunders Company—1917. Cloth. 270 pages. $1.75.

The Elements of the Science of Nutrition, by Graham Lusk. Third Edition. W. B. Saunders Company—1919, 641 pages, Cloth, Octavo.

Symptoms of Visceral Disease, by F. M. Pottenger, M. D. C. V. Mosby Company—1919. Cloth. 328 pages.

Vegetative Neurology, by Dr. Heinrich Higier of Warsaw. Translated by Walter M. Kraus, M. D., New York. Nervous and Mental Disease Publishing Company, New York and Washington—1919. Paper. 144 pages. $2.50.



Mr. J. T. Warburton, Manager. Office Entrance of the American Drug Supply Co., Distributors for G. W. Carnrick Company's products in Great Britain and Ireland, and below, Trafalgar Square, where office is located.